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Practical Pharmacy Edition

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COVER: Dr. Robert P. Fischelis, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, is shown (center) with two members of the U. S. delegation at the International Health Conference, where he is serving as an adviser. On the right is Surgeon General Thomas Parran of the U. S. Public Health Service, who was unanimously elected president of the Conference. Dr. James E. Paullin, on the left, is past-president of the American Medical Association. As far as could be learned, the A. PH. A. secretary is the only pharmacist participating in the Conference, at which representatives of approximately 67 countries set up a permanent United Nations Health Organization. Surgeon General Parran includes a discussion of proposed functions of the new organization in his paper appearing on page 352.

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ASAFOETIDA ON THE AIR WAVES

SOME proprietary manufacturers still agitate the air waves with high-pressure, low-level commercials. Last November we turned the editorial spotlight toward this contribution of radio advertising to bad public relations for pharmacy. We warned that it was time for effective self-censorship, before Washington watchdogs get more regulatory ideas of their own.

This view now appears to be shared by an organization in a strategic position. Namely, the Proprietary Association of America. At the 1946 meeting of this group, Executive Vice-President F. J. Cullen protested:

"The copy writer must realize that he and the manufacturer are assuming a great responsibility. . . must realize that they are not selling gadgets but medicines intended to relieve human suffering.

"After considering some of the copy that has been submitted to me during the past year, as well as copy which I have otherwise seen or heard," said Dr. Cullen, "I am sure that the person responsible for preparing it had not studied the product, its background and the reports of research covering the preparation with the same care that is necessary to enable him to produce material that will not deceive the purchaser."

All this from the official spokesman of the Proprietary Association should allay any suspicion that we have been hypercritical of advertising as such, or have measured radio promotion to the layman solely by the rigorous standards of science.

Proper drug advertising does and should catalyze the rational distribution of products, promote public health and create good will for the advertiser. Does today's radio advertising do the job?

At the proprietary meeting NBC President Trammell told the advertisers that on too many radio programs the commercial "fits into the show the way a riveting machine would fit into a symphony orchestra."

Injecting a bit of barbed humor into a discussion of toiletry promotion, the Scripps-Howard advertising director suggested: "We can well afford to worry about the morals of our young people more from advertising than from strong drink, when so many of us promise the young ladies in our deodorant, perfume, soap and similar copy, that if they just use these products, what happens to them that night is something that a decent girl wouldn't talk about in public."

Later we heard comment from still another quarter. Speaking before the Section on Food, Drug and Cosmetic Law of the New York State Bar Association, Surgeon General Thomas Parran of the U. S. Public Health Service took a serious view:

"In our efforts to protect the public in the manufacture of and sale of food and drugs," he said, "we cannot help feeling a deep concern over some of the advertising techniques promoting the sale of products to the general population. In this field standards self-imposed by the industries are urgently needed. I am referring particularly to the widespread use of extravagant claims and promises held out or implied in drug advertising on the radio. At almost any hour of the day, listeners may hear announcements offering relief for a wide variety of human ills. In many of these cases no factual information is supplied to limit the hopes that may be aroused by the appeals. . . a trend that in my opinion is reaching disturbing proportions."

To clean up this situation Surgeon General Parran suggested that radio might look to the example of newspapers. Many of them have gone far toward protecting the legitimate drug advertiser by keeping a firm hand on the use of their advertising space.

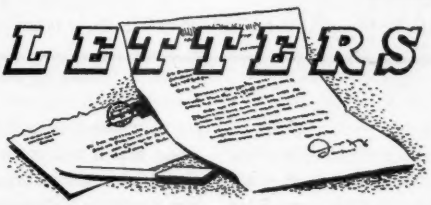
At its meeting the Proprietary Association wisely had taken the first steps in this direction. It proposed to set up a joint committee between the manufacturers and radio officials, with similar committees covering newspapers and magazines. We have a right to expect that radio, and other advertising media, will meet this proposal at least halfway to control wayward proprietary advertisers.

That the manufacturers overstepping the bounds with a "slick" view of medical product advertising are a minority does in no way reduce the need for effective control. Aside from public health considerations, it is needed to protect the manufacturer who promotes his products reputably. It is needed to protect the prestige of the retail pharmacist or the physician who is frequently dragged into the commercials as an unconsulted partner in the "recommendations" offered.

PHARMACY'S FATE IN POLAND UNDER THE NAZIS

Sirs:

During the war Germany's prime objective in Poland was to make serfs of those Poles who should escape their firing squads and concentration camps. Therefore they destroyed with real German accuracy all centres of Polish learning by murdering or deporting professors and scientists, by ransacking Polish laboratories and libraries, and by forbidding all university training.



Polish pharmacy shared the treatment of the other branches of scientific activities. Out of five Polish faculties of pharmacy, four lost everything including their buildings: Warsaw, Lwow, Poznan, Wilno. . .Warsaw is the most devastated city in the world, and everything that we pharmacists had there was destroyed. . . If these facilities are to be replaced we need every bit of aid we can get. . . In regard to libraries we have decided to approach editors of all scientific reviews on pharmacy with the warmest appeal to help Polish faculties of pharmacy to rebuild their destroyed collections. . . .

M. B. GRABOWSKI

Pharmacists who are in a position to aid the rebuilding of Polish pharmacy in any way should address Mr. Grabowski at the Polish Pharmaceutical Association Abroad, 1 Neville St., London, S. W. 7.—THE EDITOR

FROM A PHARMACY CORPS OFFICER IN GERMANY

Sirs:

Please change my mailing address for the JOURNAL. I am now assigned to the Pharmacy and PX, 97th General Hospital, Frankfurt. The pharmacy compares with the best prescription shops in the States. I get the impression here that Germans evidently have a much higher opinion of pharmacy than Americans do.

JACK W. MCNAMARA
1st Lt., P. C.

A QUERY AND A COMPLIMENT

Sirs:

Where can I buy some pectin for use in making kaolin-pectin solution for diarrhea? Question two: What is the best vehicle that may be used to put them together?. . .

While I am writing, I'd like to say thank you for the good I am getting out of the A. PH. A. JOURNAL each month. I really think that my JOURNALS are the best money I spend each year. You fellows really do a job for us in many ways. I wish every legitimate pharmacist in the U. S. A. would join up.

Big Spring, Tex. WAYNE GOUND

We are surprised that pectin N. F. is not available through your local wholesaler. Since such does appear to be the case, contact the California Fruit Growers Exchange, Products Dept., Ontario, Calif. In combining pectin with kaolin most pharmacists seem to prefer peppermint water, rather than a more viscous type of vehicle. To make the pectin easier to disperse, mix it with a small quantity of glycerin, alcohol or simple syrup before adding the peppermint water.

Our thanks for your kind comments concerning the Association's work.—THE EDITOR

ON-THE-JOB TRAINING IN HOSPITAL PHARMACY

Sirs:

. . . I enjoy very much reading the *Practical Pharmacy Edition* of the JOURNAL, and I have been especially gratified to see the section devoted to hospital pharmacy expanded.

. . . Our department has now been approved for on-the-job training for veterans. We try to give the veteran a good training in hospital pharmacy policy and administration, as well as a great deal of actual experience in manufacturing. In addition to his regular salary, the accepted veteran receives a supplementary allowance from the government which varies from $65 for an unmarried person to $110 per month for one who is married.

Ann Arbor, Mich. DON E. FRANCKE

FROM THE TROUBLED HOLY LAND

Sirs:

Binding the accumulated JOURNALS of the war years and again receiving regularly the current copies has given me so much pleasure that I want to share my satisfaction with you. . .

Those of us here who are members derive further satisfaction from noticing that the JOURNAL increases not only in the number of pages but also in its inner value.

Tel Aviv, Palestine JOSIF G. SHOR

PROTECTIVES AGAINST SUN AND WEATHER

Sirs:

The sun-tan ointment developed in the A. PH. A. laboratory for N. F. VIII is truly an elegant preparation. [See April, 1946, issue, p. 169.] Could you also give some formulas for skin protectives that may be used in winter.

Union City, N. J. DOROTHY SPECKER

Formulas of protective ointments of this type may be found on page 377, Pharmaceutical Recipe Book III.—THE EDITOR

STRAIGHT FROM HEADQUARTERS

by ROBERT P. FISCHELIS, Secretary
AMERICAN PHARMACEUTICAL ASSOCIATION

WE have reached midyear in the activities of our ASSOCIATION, and it is time to take stock of progress made in the first six months of 1946. It is also time to project plans for the remainder of the year, taking due note of the trend of national affairs in general and shaping the affairs of pharmacy accordingly.

Since January 1, 1946, there has been a very noticeable emphasis on national affairs in the thinking of the American people. Domestic affairs, such as OPA, have occupied our thoughts to a much greater extent in recent months than have our foreign relations. Domestic affairs have always been our primary concern. But the war and its aftermath taught many of us that we cannot isolate ourselves as completely from the rest of the world as some would like, because speed of travel and communication has emphasized international dependence if this world is to go on in peace.

International Health Problems

The International Health Conference now in progress in New York under the auspices of the Economic and Social Council of the United Nations is attended by delegates from 67 nations, including members as well as nonmembers of the U. N. and observers from the governing bodies of our former enemies. This is the most representative body which has ever met to consider international problems and it shows that health is a subject of world-wide interest which calls forth cooperation while other issues remain controversial. In this Conference the representatives are mostly professional and technical leaders in public health administration and services in their own countries.

It is quite certain that the constitution or charter which this Conference will adopt as a basis for the formation of a World Health Organization will be sufficiently flexible to permit the initiation of health programs having world-wide application and significance. This means that the new organization will take over the functions of the Health Office of the League of Nations which has ceased to exist. It also means that such regional organizations as the Pan American Sanitary Union will be coordinated with the World Health Organization. All nations will be in a position to call upon the new organization for advice and for guidance in health matters, to the end that public health all over the world will be improved and promoted.

Just as the League of Nations dealt with international control of narcotics and standards for drugs and biological products, so the new World Health Organization will deal with them in an advisory capacity and, as far as international trade is concerned, standards and regulatory procedure will undoubtedly be devised. It is but fitting and proper that products which could not pass the requirements of any given nation for consumption by its own people should not be offered for export without a clear understanding of the substandard nature of such products and, if such products are dangerous to health, there should be acceptable ways and means for keeping them off the market. Certainly there should be clear disclosure of the quality of these products on their labels.

Pharmacy on the Home Front

On the home front it is gratifying to be able to report that the first six months of 1946 have seen an admirable improvement in the attitude of the U. S. Civil Service Commission, U. S. Army, U. S. Navy, U. S. Public Health Service and Veterans Administration toward the part that pharmacists can play in the health functions for which these Services are responsible. Not only is this gratifying from the point of view of supplying more adequate pharmaceutical service, but also because it will raise the economic status of the pharmacists in the government service and this will be reflected, in turn, in better hours and pay for pharmacists in civil life.

Relations with other professions, notably medicine, are very much on the up-grade as we enter

into the second half of 1946. The *Journal of the American Medical Association* has printed a number of editorials calling attention to problems dealing with prescribing and labeling which have shown an appreciation of the difficulties confronting pharmacists in their relations with physicians. Moreover, conferences with representatives of the Council on Pharmacy and Chemistry have become more frequent and have covered such subjects as promotion of the use of the metric system in prescribing, the new therapeutic trials program of the A.M.A., the regulation of the distribution of barbiturates and the publication of the Council Reports in our own JOURNAL.

Looking Ahead

Looking ahead we see the necessity for constructive activity in determining policies with regard to:

1. Enrollment of students of pharmacy
2. Improvement of pharmacy faculties
3. Control of outlets for the distribution of drugs
4. Control of distribution of barbiturates
5. Distribution of information on programs for promoting better relations between state medical and pharmaceutical associations
6. Uniformity in state legislation bearing on the practice of pharmacy and the regulation of the production and distribution of drugs, devices and cosmetics
7. Sickness insurance with special reference to the extent and method of coverage of pharmaceutical services
8. Acceptance of a place in the proposed medical service units in the Army and Navy
9. Greater use of the facilities of the AMERICAN PHARMACEUTICAL ASSOCIATION in accomplishing the objectives of American pharmacy
10. The national pharmaceutical survey now in progress under the aegis of the American Council on Education.

All of these topics will come up for discussion and action at the Pittsburgh meeting of the A. PH. A. Your point of view and your constructive aid are needed in arriving at the correct solution.

℞

A. M. A. COMMENTS ON THIOURACIL WARNING

THAT the medical profession is not particularly pleased with the idea of having warning notices not directed by the physician appear on prescription labels, and that A. M. A. officers realize that pharmacists are not responsible for such action in the case of thiouracil, is brought out in the following editorial from the *Journal of the American Medical Association* (131: 524, 1946):

"The Food and Drug Administration has announced that pharmacists who dispense thiouracil on prescription must place a warning on the label cautioning the patient that this drug may impair resistance to infection and suggesting that the patient should report to his physician immediately at the first sign of fever, sore throat or other symptoms of a cold. The Federal Food, Drug and Cosmetic Act exempts drugs dispensed on a written prescription of a physician from bearing a statement of the quantity of contents and a statement of the active ingredients on the label. The law does not, however, exempt such drugs from the requirement that the labeling bear adequate directions for use or warnings necessary for the protection of users.

"Thiouracil is a dangerous drug and may cause drug fever, skin rashes, leukopenia and agranulocytosis. The most important step in treatment of the complications of thiouracil is early recognition of the complications and prompt institution of appropriate therapy.

"The Food and Drug Administration is reported to have consulted with experts experienced in thiouracil treatment and to have stated that the consensus of these experts favored the placing of a warning to the patient on the label of the drug when dispensed on prescription. This warning apparently is intended to supplement and reinforce warnings given orally by the physician. Physicians should recognize that the pharmacist is required by federal law to place this warning on the label of the drug, even though it has been dispensed on written prescription. This requirement on the part of the pharmacist may disturb normal pharmacist-physician relationship unless the physician is aware of the ruling. Presumably the ruling is intended to prevent, as much as possible, needless deaths from this useful but potentially dangerous drug."

PRESENT STATUS OF TYROTHRICIN FOR TOPICAL USE*

AS COMPLEMENT TO SYSTEMIC ANTIBIOTICS, DRUG PRESENTS ADVANTAGES OF WIDE RANGE OF EFFECTIVENESS LOCALLY, GOOD STABILITY AND SAFETY

BECAUSE tyrothricin appeared to offer promise as a therapeutic improvement over the sulfonamides and certain other antibacterial agents for topical application, and as a means of avoiding dangers possibly inherent in the indiscriminate use of sulfonamides and penicillin, the desirability of utilizing this agent for topical antisepsis was investigated.

Tyrothricin is a mixture of two substances, gramicidin and tyrocidine. That it exerts an antibacterial action against a large number of organisms is well established, although no study defining the exact extent of the bacterial spectrum for tyrothricin has as yet been reported. Unfortunately, most of the published reports concern a limited group of organisms and none presents a comprehensive review of the problem. The data obtained by different investigators are not always comparable since the medium used and the cultural conditions under which the tests were performed vary widely.

In cooperation with Dubos, a systematic survey of the effect of gramicidin and tyrothricin on a large variety of microbial species under standardized conditions was undertaken.[1]

The tests were carried out in a medium containing 1% serum albumin. It is well known that most antiseptics are inhibited in their action against bacteria by proteins in general and by serum proteins in particular. It was considered, therefore, that an inhibition test carried out in a medium containing a large amount of serum albumin would resemble more closely conditions prevailing in exudates than would be the case in a medium free of proteins.

Gramicidin is unaffected in its antibacterial action by any concentration of serum albumin. In fact, as observed by Dubos, its activity seems to be appreciably increased in this medium. On the contrary, tyrocidine, the other component of tyrothricin, is, like other antiseptics, largely inhibited by albumin.

Although this survey is far from complete, the results at the present time permit a few statements which are summarized in Table I. The data presented deal with gramicidin. The comparative figures for tyrothricin would be two to five times larger. Tyrothricin contains approximately 20 to 25% gramicidin, and some 60% tyrocidine. Although the latter substance also exhibits marked antibacterial activity *in vitro*, most of this activity is lost in the presence of animal tissues; this is probably due to the fact, already mentioned, that tyrocidine is inhibited by serum proteins. Most of the *in vivo* activity of tyrothricin therefore is due to its gramicidin content.

Furthermore, the data presented in the table refer to bacteriostatic levels. Gramicidin does not

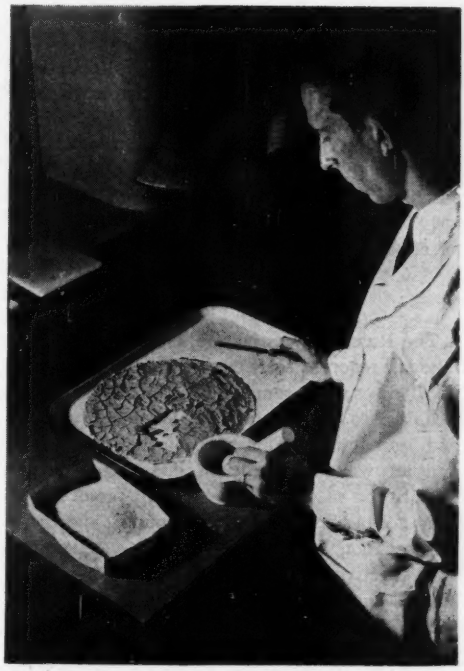
* Condensed from a paper by John Henderson, M.D., appearing originally in the *Scientific Edition* of THIS JOURNAL, 35: 141, 1946. Received from the Department of Clinical Research, Johnson and Johnson, New Brunswick, N. J.

kill the spores of aerobic or anaerobic sporulating bacilli, but only inhibits their multiplication. In the case of a few nonsporulating species (group D streptococci in particular) the effect of gramicidin is essentially bacteriostatic. In general, however, the bactericidal level is very close to the bacteriostatic level and this is particularly true in the case of the pathogenic species tested.

An interesting comparison of the relative speed of tyrothricin and penicillin in killing a standard strain of *Staphylococcus aureus* was made by Crowe, Fisher, Ward and Foley.[2] A series of pour plates were made at varying intervals of time after inoculating with one drop of a twenty-four hour Staphylococcus culture, a 5-cc. broth tube containing tyrothricin in a concentration of 1:20,000. Those poured within two to three minutes after inoculation showed a marked reduction in the number of organisms, and the plate poured at the end of one hour was sterile. The penicillin plates, on the other hand, showed no decrease in the number of organisms after one hour. A sharp reduction, however, occurred between the third and sixth hours and the twenty-four hour plate was sterile.

The antibacterial effect of tyrothricin under clinical conditions has been extensively investigated. Rammelkamp[3] used tyrothricin in the treatment of 58 localized infections and demonstrated that when applied to chronic ulcers of the extremities, tyrothricin resulted in sterilization and healing if the local infection was caused by *Streptococcus hemolyticus*, *Staphylococcus aureus* or *Streptococcus faecalis*. He also noted encouraging results upon application of this substance to mastoid cavities following mastoidectomies. Staphylococcic empyema and pneumococcic empyema responded poorly, whereas in one patient with streptococcic empyema the response was dramatic.

Herrell[4] believes that the best results are obtained in cases of ulcers infected with *Streptococcus pyogenes*, and that the results against *Staphylococcus aureus* are not quite so satisfactory. In one series of 93 cases suffering from infected ulcers and wounds, reported from the Mayo Clinic, failures occurred in 17.[4] The response in more than half of the remaining cases could be considered good or excellent. Francis[5] reports a



Photos, Sharp & Dohme Laboratories

TO PRODUCE TYROTHRICIN, liquid bouillon is inoculated with Bacillus brevis, a soil organism, then incubated in tray fermenters like those shown at the left. When the culture has been harvested, tyrothricin is precipitated out, purified and dried. Some of the crude, dried product can be seen on the tray, above. After it has been finely powdered, the drug must be defatted with ether, processed further, standardized, and sterilized by candle filtering.

TABLE I.—PARTIAL LIST OF ORGANISMS INHIBITED BY GRAMICIDIN

Organism	Concentration of Gramicidin Required to Inhibit Growth (γ/Cc. of Broth Containing 1% Serum Albumin)
Diplococcus pneumoniae	0.005– 0.02
Streptococcus hemolyticus (groups A, B, C)	0.001– 0.05
Streptococcus hemolyticus (group D) including *Enterococcus* and *Streptococcus faecalis*	0.05 – 0.2
Streptococcus anaerobius	0.01 – 0.02
Lactobacillus	0.05 – 0.5
Staphylococcus aureus	0.5 – 5.0
Corynebacterium diphtheriae and diphtheroid bacilli	0.05 – 0.5
Mycobacterium tuberculosis	0.02 – 0.05
Bacillus anthracis	5.0 –20.0
Saprophytic aerobic sporulating bacilli	0.1 – 1.0
Clostridium tetani and other anaerobic sporulating bacilli	0.02 – 0.5
Neisseria gonorrheae	0.5 –10.0
Neisseria meningitidis	0.5 –10.0
Gram-negative bacilli	No inhibition

case of a sulfonamide-resistant infection with *Streptococcus pyogenes* which responded satisfactorily to local applications of tyrothricin, and Rankin[6] reported excellent results from the use of tyrothricin in five or six cases of chronic ulcer.

Kvale, Barker and Herrell,[7] as the result of an extensive study of ulcers of both ischemic and stasis origin,* believe that tyrothricin is particularly valuable and were impressed by its low toxic effect on the extremely delicate tissues concerned

Other Clinical Results

The Russian investigators, Gause and Brazhnikova,[8] reported their clinical results in a series of 573 cases with gramicidin S, a substance which is similar to tyrothricin but is less highly refined and less active. This series included infected gunshot wounds, empyema and osteomyelitis. Application of gramicidin S led to rapid disappearance of bacteria from the wounds, and these workers thought that the substance was particularly effective in preparing these wounds for subsequent surgical treatment.

Tyrothricin has proved useful in the preparation of infected ulcers and wounds for skin grafting and frequently facilitates the eradication of stubborn bacterial infections, thereby hastening the possibility of early grafting.[9]

The use of tyrothricin in the treatment of diseases of the nose and throat has been reported by Schoenbach, Enders and Mueller,[10] who observed some partial effect upon streptococcus carriers, but not complete sterilization. Lindsay and Judd[11] investigated in considerable detail the possible value of tyrothricin in the treatment of chronic infections of the upper part of the respiratory tract, and for elimination of pathogenic bacteria from the tonsils of carriers. It was not evident that the duration of the infection was shortened by the use of tyrothricin, nor did the substance appear to alleviate the symptoms. Likewise, there was little evidence that improvement following the use of tyrothricin for chronic infection of the sinuses was any more rapid than customarily follows conservative treatment.

On the other hand, Crowe and his associates[12] used tyrothricin locally in the treatment of acute otitis media, acute and chronic mastoiditis, and acute and chronic sinusitis, for over two years and felt that they obtained better results in many cases than with other forms of treatment

Tyrothricin has also been used for the treatment of such miscellaneous conditions as keratoconjunctivitis, pneumococcal conjunctivitis,[12] treatment of Gram-positive bladder infections by instillation, and certain cases of pyodermatitis.[3] Piper[13] has found the material effective in treatment of coccal and certain mixed infections of the vagina, but it is doubtful that it is clinically effective against trichomoniasis.

The remarkable effects of tyrothricin in the treatment of bovine mastitis have been applied on a very large scale in the field and should be mentioned, since this work, which has been presented in great detail by Little, Dubos and Hotchkiss,[14–17] was largely responsible for attracting attention to tyrothricin for use in human medical fields.

The optimal therapeutic concentration of tyrothricin, taking into consideration the local tissue toxicity and the maximal antibacterial effect, as originally demonstrated by Herrell and Heilman,[9, 18–20] is in the neighborhood of 500 micrograms per cubic centimeter. This concentration is widely used today for therapeutic application, and was adopted as the basis for calculating the amount to be impregnated per unit area of gauze in the manufacture of adhesive compress dressings.

Gauze is impregnated with tyrothricin in a manner such that, as the gauze becomes wetted, the tyrothricin automatically forms a solution in the tissue fluids of approximately optimal concentration. That it exerts well-marked bacteriostatic and bactericidal effects is readily demonstrable.*

Bacterial Fastness

Some question may be entertained concerning the development of tyrothricin-fast strains of bacteria as this agent comes to be used by large masses of the population. Such a phenomenon is, of course, theoretically possible, as bacterial fastness may be developed under certain conditions against almost any agent. In the case of tyrothricin, it is unlikely that such a phenomenon could be of practical significance. The development of fastness to tyrothricin by a chance organism contaminating a specific wound would be a matter of purely local concern in the treatment of a particular wound. This is true because there would be little possibility of such a tyrothricin-fast organism being disseminated and becoming established as a tyrothricin-fast strain among the population. Even though a given organism did become tyrothricin-fast, and subsequently caused a systemic infection, the fact would be of little material significance since some agent would of necessity be used because tyro-

* Ischemic refers to local deficiency of blood usually due to contraction of a blood vessel as compared with stoppage of the blood, or stasis.

* For data, see original paper in the *Scientific Edition* of THIS JOURNAL, 35: 141, 1946.

thricin cannot be used systemically. For this reason, tyrothricin is unique in that the theoretical possibility of the development of bacterial fastness to this compound is of little epidemiologic significance.

Many antibiotic agents have proved of no practical use because of toxicity, even though some have exhibited a high degree of antibacterial activity. It is therefore of importance to consider tyrothricin from the standpoint of possible toxic manifestations before reaching a final conclusion regarding this substance.

Low Tissue Toxicity

That tyrothricin possesses a remarkably low local tissue toxicity was first demonstrated by the tissue culture studies of Herrell and Heilman.[18–20]

Dubos and Hotchkiss,[22] in studying the components of tyrothricin, reported that high concentrations of gramicidin did not affect the oxygen uptake of polymorphonuclear cells, whereas similar concentrations of tyrocidine caused cessation of cell respiration and disintegration of white cells. Subsequent studies by Heilman and Herrell[19, 20] showed that gramicidin, on the other hand, was more toxic than tyrocidine and that the cytotoxicity of tyrothricin was largely due to its content of gramicidin.

It should be emphasized, however, that when the cytotoxicity of gramicidin or tyrocidine is compared with that of other germicides commonly used for local application, such as zephiran, merthiolate or phemerol, these components of tyrothricin are found to be considerably less toxic under the same conditions.[20]

The acute toxicity of tyrothricin and its fractions for animals has been reported by Robinson and Molitor.[23] They found that the daily parenteral administration to dogs of 2 mg. of gramicidin or tyrothricin per kilogram of body weight produced death in from two to eight days, but these substances were not toxic on oral administration. Gramicidin does not appear to be inactivated in the stomach, but the presence in the intestines of large amounts of Gram-negative organisms causes inhibition. There is little evidence that any therapeutic effect may be obtained by oral administration, although under experimental conditions, with the adequate feeding of gramicidin, a definite effect on the Gram-positive flora can be recognized.

The most striking toxic manifestation of tyrothricin is its hemolytic effect upon the red corpuscles when the material is injected experimentally into animals by the intravenous route.

This phenomenon constitutes the principal reason that tyrothricin cannot be used parenterally; however, it is of no moment when tyrothricin is used topically or in the treatment of body cavities not directly connected with the circulatory system, or in the treatment of open wounds.

Even in the latter case, should active bleeding be present, no absorption of the tyrothricin would be expected, since whatever tyrothricin were present would be washed away by the flow of blood before any absorption into the blood stream could occur; in any event, the amounts of tyrothricin present would be too small to exert any untoward effect.

Of importance is the question of possible sensitization to this substance. In reviewing the literature pertaining to tyrothricin, one is impressed with the paucity of reports concerning untoward manifestations resulting from the topical application of this material, in therapeutic concentrations, either to the body integument or various physiologic or artificial cavities.

Sensitivity Very Rare

In so far as we have been able to ascertain, no instance of tyrothricin sensitivity has been reported, although the compound now has been used in a wide variety of conditions and applied by a number of different methods and vehicles over a period of several years. It is interesting to note that during the last two years tyrothricin has been produced in ever-increasing quantities and is being dispensed widely for a variety of purposes.

Grolnick[24] has exhaustively studied the question of whether tyrothricin was capable of causing sensitization. In 171 subjects on whom a solution of tyrothricin containing 1, 2, 5 or 10 mg. per cc. had been applied by patch test for a two-day period, there was no evidence of primary irritation. Twenty-five subjects who had been treated by a seven-day application with a solution containing 10 mg. per cc. did not become sensitized to tyrothricin.

Finally, sensitivity to tyrothricin failed to develop in 41 subjects who had been given repeated applications with adhesive compresses impregnated with tyrothricin, over a prolonged period.

Keefer[25] found no positive reactors in 105 patch tests, and Cooke and Finkelstein[26] tested a total of 82 subjects without observing evidence of sensitization.

It may be concluded with reasonable safety, therefore, that although sensitivity is not uncommon in the case of the sulfonamides, penicillin and certain antiseptics, tyrothricin has not pro-

duced sensitization of the skin under conditions of the experimental studies so far carried out. If it occurs clinically, experience would seem to be sufficiently large to warrant the conclusion that it must be very rare. However, were sensitivity to occur occasionally, this probably could not be considered of such serious consequences as would pertain in the case of the sulfonamides or penicillin, since tyrothricin is never administered systemically and sensitization would, therefore, be merely a matter of local contact and of no permanent significance.

Summary

Tyrothricin is useful against a wide range of organisms when applied topically, and in this respect its use should be considered complementary to that of the systemic antibiotics.

It possesses advantages for topical use, over certain other antibacterial agents including the sulfonamides and penicillin, because of its stability, a wide spectrum of antibacterial activity, maintenance of potency in presence of blood and serum, low tissue toxicity, and lack of sensitizing properties.

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A. PH. A. ISSUES ANALYSIS OF PRESENT BARBITURATE LAWS

A comprehensive analysis of present barbiturate regulation is presented by Dr Robert P. Fischelis, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, in the *Scientific Edition* of THIS JOURNAL (35: 193, 1946). The report represents part of the study being made under the auspices of A. PH. A.'s Committee on Legislation. A model state barbiturate bill also has been drafted by the Committee, and will be presented for approval at the A. PH. A. Convention.

Although all but 12 states now have some form of control over barbiturates, the study shows, there is a wide disparity in effectiveness and coverage. States that have no laws or regulations on the subject are Arizona, Idaho, Illinois, Iowa, Kentucky, Massachusetts, New Mexico, Ohio, South Dakota, Texas, Wisconsin and Wyoming.

All but one of the 35 laws now in effect restrict the sale of barbiturates, or barbiturates and other drugs, to prescriptions. In New Hampshire, an exception, the general law on potent drugs limits the sale of all such drugs to a registered pharmacist or assistant pharmacist.

Fifteen of these laws make no reference to the refilling of prescriptions, with restrictions varying in other states up to a blanket prohibition on refills found in five laws.

Penalties for violations also serve to illustrate the wide range of legal control in different parts of the country. Fines extend from a minimum of $10 to a maximum of $10,000, and prison terms vary from a minimum of ninety days to a maximum of five years.

The A. PH. A. study classifies existing laws in detail as regards type, scope, restriction to prescriptions, renewals, regulation of sales by manufacturers and wholesale druggists, labeling, exempt preparations, and dispensing by physicians, dentists and veterinarians.

AAAS PHARMACY SUBSECTION

The Subsection on Pharmacy of the American Association for the Advancement of Science will present a program at the organization's meeting in Boston, December 26–31. Those wishing to present a paper in the fields of pharmacy, pharmaceutical chemistry, pharmacology or pharmacognosy should submit the title of the paper at once to the Subsection chairman, Dr. Glenn L. Jenkins, Purdue University School of Pharmacy, Lafayette, Ind.

BRITISH HONOR U. S. PHARMACIST

THE BRITISH AMBASSADOR, Lord Inverchapel, congratulates Maj. Woodrow C. Herbert of the Pharmacy Corps following presentation of the Order of the British Empire.

THE "Most Excellent Order of the British Empire" was bestowed upon Maj. Woodrow C. Herbert of the Army Pharmacy Corps at ceremonies in Washington, D. C., on July 11. Lord Inverchapel, the Ambassador, presented the decoration in behalf of King George VI at the British Embassy, citing Maj. Herbert as a "tireless worker who laboured unceasingly in connection with supply of medical stores for relief of the civil population" in Greece. "It was largely due to his untiring efforts that the issue and distribution of medical supplies to the civil hospitals, both permanent and improvised, was maintained during the armed rebellion.... Working extremely long hours day in and day out, he set an outstanding example to both military and civil personnel of devotion to duty without thought of self. He was often under fire during the hostilities, and throughout showed complete disregard for his personal safety."

The pharmacist thus honored had been selected in 1944 to serve as medical supply officer with an organization formed to take supplies to beleaguered Greece. The British in Egypt had laid plans for the project, which was originally to have included Albania and Yugoslavia as well. Since part of the supplies came from the United States, it was decided that a small contingent of American specialists should participate in the mission.

In October, 1944, the supply forces left Egypt for Greece, with Maj. Herbert in complete charge of the medical supply program for the civilian population. Conditions were chaotic, with a minimum of qualified personnel and equipment. When distribution bogged down, Maj. Herbert commandeered every available type of transportation—burro, truck, train and boat—to move medical stores from the 12 ports receiving them.

With supplies trickling in from other organizations, such as Greek War Relief and the Greek, Swiss and American Red Cross organizations, it soon became apparent that distribution was

neither equitable nor well coordinated. Maj. Herbert therefore took the lead in establishing the Joint Medical Supply Committee of Greece, which coordinated all efforts to bring relief to the Greek people. As an outgrowth of this, he set up a Joint Medical Supply Depot as a central point of distribution.

When civil war came to Greece, Maj. Herbert and his associates in the medical supply program often worked under constant fire fifteen to eighteen hours a day to bring aid to the ill and wounded.

After the civil war, in April, 1945, Maj. Herbert was forced to return to America because of ill health. Civilian medical supply work in Greece was continued by an American pharmacist with UNRRA, Vincent Norelli.

Before entering the Army, Maj. Herbert had practiced as a retail pharmacist in Salt Lake City, Utah. In 1940 he was commissioned in the Medical Administrative Corps., later transferring to the newly established Pharmacy Corps. Originally a post exchange officer, he soon entered medical supply. After serving in the Army Laboratory in New York, he went to the Medical Field Service School at Carlisle Barracks, Pa. When LaGarde General Hospital in New Orleans was first opened, Maj. Herbert was on hand to inaugurate the medical supply service. From there he went to the Medical Section of the Utah ASF Depot at Ogden. August, 1943, found Maj. Herbert overseas to take charge of all medical supply work in Central Africa.

His later achievements in Greece won him the Order of the British Empire, with rank of Honorary Member, climaxing this Army career of a pharmacist. Maj. Herbert, who is a member of A. PH. A., now serves as director of the Stock Control Division of the St. Louis Medical Depot, nerve center for the distribution of drugs and medical supplies to American forces throughout the world.

FIRST PROJECTS APPROVED FOR SURVEY

PROJECTS relating to the testing of the abilities and achievements of pharmacy students and to qualifications for the faculties of pharmacy schools have been recommended by the Committee on Pharmaceutical Survey to receive first attention in the nation-wide study of pharmaceutical education, practices and services announced in the July issue of the JOURNAL.

The survey is being conducted by the American Council on Education, which announces the following Committee on Pharmaceutical Survey to serve as the advisory group:

George D. Beal, assistant director, Mellon Institute; W. Paul Briggs, Veterans Administration; W. W. Charters, *chairman*, director, The Research Service, Stephens College; B. V. Christensen, dean, College of Pharmacy, Ohio State University; Donald A. Clarke, apothecary-in-chief, The Society of the New York Hospitals; George V. Doerr, McKesson and Robbins, Inc.; A. G. DuMez, *vice-chairman*, dean, School of Pharmacy, University of Maryland; Carson P. Frailey, executive vice-president, American Drug Manufacturers Association; H. Evert Kendig, dean, School of Pharmacy, Temple University; Frank W. Moudry, secretary, Minnesota State Board of Pharmacy; Edward S. Rogers, chairman of the Board, Sterling Drug, Inc.; Robert L. Swain, editor, *Drug Topics;* Frank O. Taylor, Parke, Davis & Company; John A. Stevenson, president, The Penn Mutual Life Insurance Company; Charles R. Walgreen, Jr., president, Walgreen Drug Company.

Also in attendance at the meeting were:

George F. Zook, president, American Council on Education; A. J. Brumbaugh, vice-president, American Council on Education; E. L. Newcomb, secretary, American Foundation for Pharmaceutical Education; Edward C. Elliott, director, The Pharmaceutical Survey; Alice L. Richards, executive assistant to the director.

It is expected that this Committee will create a number of consulting subcommittees representing various interests concerned with the survey.

In addition to recommending initial projects at its meeting on June 26, the Committee considered detailed plans for the three-year study, presented by the director, Dr. E. C. Elliott. Other projects approved include development of standards for the selection and admission of pharmacy students, and for the guidance of students; a spot analysis of present-day prescriptions to determine the knowledge required by the pharmacist for compounding; and an analysis of the activities engaged in by pharmacists—professional, commercial and civic.

PHARMACOLOGY OF Laxatives

by MELVIN W. GREEN

CHAIRMAN, COMMITTEE ON PHARMACEUTICAL RECIPE BOOK

MISUSE OF LAXATIVES IS DUE TO MISCONCEPTION OF CONSTIPATION.. LIMITATIONS, AS WELL AS MODE OF ACTION AND RATIONALE, SHOULD BE WELL UNDERSTOOD IN DISPENSING THESE WIDELY USED REMEDIES

THE pharmacist dispenses more laxatives annually than any other type of household remedy. In a typical year, 1933, it was estimated that over 20 million dollars worth of these drugs was purchased in the United States. Because laxatives are so widely used it is important that the pharmacist be well informed concerning their use, mode of action and limitations.

For a very long time it has been the popular belief that a bowel movement daily is essential to good health. Most physicians, on the contrary, believe the normal interval between movements varies considerably for different persons. Of the thousands of persons attempting to establish a daily cycle with the use of laxatives, many obviously do not actually know what their own optimum schedule is.

The use of laxatives often contributes to irregular bowel movements since a cathartic may virtually empty the bowel and the patient can therefore have no movement the following day, a fact which he often attributes to constipation. It is not so much frequency of bowel movement, but character of the stool and ease of defecation which determine constipation.

The fact that laxatives must be used with caution is reflected in the labeling requirements of the Food and Drug Administration. The danger lies largely in the abuse of laxatives during periods of abdominal inflammation, particularly appendicitis. It is significant that in one study of a series of cases of appendicitis, 1 out of 96 patients with acute appendicitis died if no purgative were taken, 1 out of 11 died if a purgative had been taken, and 1 out of 4 died if the patient had taken laxatives repeatedly [A. E. Smith, *Hygeia*, 23: 415, 1945].

Although the use of laxatives has undoubtedly been abused and their use is often clearly an economic waste not without danger, they do have well-defined uses in the practice of medicine. Some of these uses are as follows:

1. In cases of drug or food poisoning, the saline cathartics are especially useful in clearing the gastrointestinal tract of the poison.
2. It is often essential to administer cathartics after anthelmintics to free the body of both the anthelmintic and the worm.
3. In edema, the saline cathartics are often of value in eliminating water more rapidly.
4. Castor oil in conjunction with quinine and pituitrin is sometimes prescribed to induce labor.
5. Diagnosed constipation.

Many attempts to classify cathartic drugs have been made, some schemes breaking down according to the type of substances, others depending on the character of the physiological response. Differentiation into laxatives, purgatives and cathartics is apt to be of more academic interest than practical application. The author finds the following scheme of classification to be helpful:

A. BULK-INCREASING LAXATIVES

1. Cellulose and non-digestible polysaccharides (mucilages).
2. Saline cathartics.
3. Liquid petrolatum.

B. IRRITANT CATHARTICS

1. Vegetable acids and sulfur.
2. Castor oil.
3. Anthraquinone cathartics and phenolphthalein.
4. Drastic purgatives.
5. Mercurial purgatives.

Bulk-Producing Laxatives

Everyone is familiar with the fact that cellulose in the form of the crude fiber, etc., of vegetables and fruit produces catharsis by virtue of its bulkiness. Somewhat analogous substances, certain mucilages, have been used for this same purpose. These mucilages, when moistened, form gels with great bulk which extends the gut sufficiently to encourage peristalsis. The advantage of these substances is the relative freedom from irritation.

It is important that the user be instructed to add sufficient water or milk to these mucilages so that they are completely gelled before administration. Considerable damage could be done by the dry powder absorbing water and swelling while in the esophagus.

Drugs in this class are agar, psyllium seeds, karaya gum, and possibly methyl cellulose.

LIQUID PETROLATUM has been used for many decades as an emollient cathartic. It lubricates the feces and prevents too much dehydration. At first believed to be the safest of all laxatives, it has since been shown to be disadvantageous because of its interference with the absorption of fat-soluble vitamins from the intestine. This has been shown to be true for vitamins A and D, and it probably is true for vitamin K also. Although not as thoroughly studied as it might be, there is considerable evidence that the continuous use of "mineral oil" is not in the interest of good nutrition.

Recently Sodeman and Stuart [*Ann. Internal Med.*, 24: 241, 1946] have studied 264 lipoid pneumonia cases resulting from liquid petrolatum between 1927 and 1942. It is of interest that nearly half of the adult cases could be attributed to the use of mineral oil as a laxative.

Liquid petrolatum is useful in cases where soft stools and the avoidance of straining are necessary, such as in hypertension, hernia, embolisms in the brain area, and hemorrhoids.

SALINE LAXATIVES, like sodium sulfate and magnesium sulfate, increase bulk by their ability to increase the water content of the intestines, osmotically. In fact, a study of the mode of action of this group of drugs is an excellent lesson in the principles of osmotic behavior.

If a hypertonic solution of sodium chloride is in contact with the intestine it does not remain hypertonic long. The intestine, being permeable to both sodium ions and chloride ions, soon absorbs enough of the salt to render the solution isotonic and no purging takes place. If a solution of sodium sulfate is placed in the gut, a different condition exists. The intestine is permeable to sodium ions but not to sulfate ions. The sulfate ions (and enough positive ions to balance it) stay behind creating a hypertonic state. This can be alleviated only by the introduction of water from the blood and other tissues until the fluid inside the intestine is again isotonic. The increased pressure of this extra water, by virtue of its bulk, brings about catharsis. This is what happens when the physician prescribes a saline cathartic during edema; the water from the edematous area enters the gut to render its contents isotonic.

Any simple inorganic compound can behave as a saline cathartic providing the intestine is impermeable to one or more of its ions. Compounds like magnesium sulfate, in which neither ion can penetrate the intestine in appreciable amounts, are very effective, although not necessarily more so than compounds in which only one ion is not absorbed.

The frequent use of salines is naturally inadvisable when it increases the possibility of dehydration.

Irritant Cathartics

All drugs in this category are irritating to the mucosa of the intestine and the irritation increases the peristaltic activity, thus encouraging defecation. Some of the drugs, like those of the anthraquinone group, confine most of their irritating action to the colon, while others like the drastic resinous purgatives, irritate the entire intestinal tract.

VEGETABLE LAXATIVES AND SULFUR. Many organic acids contained in such fruits as figs and prunes are mild laxatives. Recently Gold and co-workers have shown that fumaric acid and its salts are excellent mild laxatives without the nephrotoxic action of tartrates [THIS JOURNAL, *Sci. Ed.*, 32: 173, 1943].

Sulfur is inert, but in the intestinal tract

bacteria produce a small quantity of hydrogen sulfide which is a mild irritant.

CASTOR OIL. Castor oil of good quality is nonirritant until hydrolysis takes place in the intestinal tract, liberating ricinoleic acid, an hydroxy fatty acid, which is irritating and causes peristalsis. If free ricinoleic acid is present in the original oil, irritation of the stomach causes nausea and vomiting. In the days before good refining methods, castor oil was the bane of children because of the nausea from this cause.

ANTHRAQUINONE PURGATIVES. Senna, rhubarb and cascara owe their activity to anthraquinone compounds such as emodin, chrysophanic acid and isoemodin. These compounds, individually and in the free state, are not very active due to absorption and the need for their synergistic combination.

The drugs in this group can cause catharsis only after a considerable time because they act largely on the colon and a number of hours are required for their arrival at that point. As a rule they are administered at night for action the following morning.

Cascara sagrada is the mildest of these drugs, has a mild tonic action to the gut and does not leave the gut in such a state of disequilibrium after its action as some irritant cathartics.

Senna causes considerable more griping and is usually prescribed with carminatives and other adjuvants in an attempt to lessen this effect.

Rhubarb contains tannin which often leads to constipation afterward. This is alleged to be a virtue in treating diarrhea, *i. e.*, the cathartic eliminates the poison after which the tannin stops the diarrhea.

Because of the griping effects of most of the drugs in this group, drugs like atropine (and belladonna) and strychnine have been added as "correctives." The remnants of this belief still are evidenced in some of the National Formulary pills. This use is irrational, for the "correctives" act in a comparatively short time, while the cathartics often remain inactive for eight hours or more.

PHENOLPHTHALEIN. Phenolphthalein behaves very much like the anthraquinone purgatives. It is insoluble in the acid contents of the stomach, but in the alkalinity of the intestine and aided by the bile, it dissolves. Only about 15% of a therapeutic dose is absorbed and it is excreted largely by the kidneys in a combined form. A portion is excreted in the bile. The compound is so free from toxicity that Fantus was unable to determine a toxic dose in animals.

In hypersensitive individuals, the drug may lead to excessive purgation, colic, palpitation, labored respiration, and possibly collapse. Very frequently a skin rash develops in persons not unduly sensitive to the drug otherwise. The skin lesions often leave persistent pigmented areas which exist for months or even years.

MERCUROUS CHLORIDE (*calomel*). It has not been so many decades ago when medicine could not be practiced without calomel, a drug which is considered dangerous today. The great virtue of calomel was thought to reside in its ability to stimulate bile secretion by the liver. The green color of the stools was considered evidence of this. Modern experimentation has shown this conception to be false. The calomel is antiseptic in action and thus prevents the destruction of the bile pigment, biliverdin, and further, the cathartic action propels the biliverdin forward before it can change in the normal fashion to bilirubin. The net result is a greenish stool.

Mercurous chloride is so insoluble that too few ions are present to be active until, in the intestinal environment, a small amount is converted to more soluble forms, probably the oxide. The mercury ion irritates the musculature, and brings about increased peristalsis. Should this fail to take place, enough mercury may be absorbed to prove toxic. Consequently a saline cathartic is given at the finish of the "course" of calomel. We are faced with the paradox of a cathartic used to eliminate a cathartic!

IRRITANT RESINS. For a number of decades, the resinous drugs, jalap, podophyllum, ipomea and colocynth have been used as drastic purgatives. These potent resins are irritant to the entire intestinal tract. Usually they pass through the intestine so rapidly that they have no opportunity to do much harm, but in the presence of mechanical bowel obstruction or if for any other reason their exit is delayed, the inflammation may cause serious damage.

Recently advantage has been taken of the irritant quality of podophyllin (resin of podophyllum) for the removal of venereal warts.

Irritant cathartics are undesirable at any time, but particularly those acting on the colon must be omitted during pregnancy as they are capable of causing miscarriage.

To recapitulate, cathartics fall into several classes with different modes of action. A better knowledge of their action shows them to be abused frequently because of failure to appreciate their limitations. Pharmacists could do a public service by keeping their patrons informed and by encouraging them to see physicians to have their constipation "confirmed" by a correct diagnosis.

FIRST COURT TEST...

FDA RETAIL JURISDICTION UPHELD

THE Food and Drug Administration's contention that pharmacists must comply with the Federal legislation when dispensing drugs obtained through interstate commerce has been upheld by a District Court decision in Columbus, Ga. The case has special significance since it is the first charge of misbranding on an over-the-counter sale that has been contested. A number of retail pharmacists were fined previously for a similar offense but did not contest the charge.

In brief the court decision holds that Congress intended that the Act should prevent misbranding by the pharmacist while a product (received in interstate commerce) is being held for sale, and that such regulation is Constitutional. It gives additional legal support to FDA requirements that pharmacists observe the prescription legend and dispense over-the-counter products with adequate directions and warnings.

This applies to drugs dispensed in the same form or with the same identity as received in interstate commerce. The case does not clarify the status of an over-the-counter product for only local distribution that has been made by a retail pharmacist from two or more ingredients received in interstate commerce. Many persons in the drug field believe that such a mixture becomes a new product which is not under Federal jurisdiction because it has not been in interstate commerce.

In the Georgia case, a pharmacist, Jordan J. Sullivan, received from a local distributor a bottle of sulfathiazole tablets originally shipped from Illinois. The tablets were properly labeled, including the prescription legend and a warning concerning toxic reactions. Subsequently, the defendant on two occasions allegedly sold some of the tablets over-the-counter under his own label. In one instance the dispensing container was labeled solely with the word [*sic*] "Sulfothiazal," and, on the second offense, solely with the word "Sulfathiazole."

The government charged that the drug had been misbranded under the Act since it bore neither adequate directions nor warnings.

The defendant maintained that the allegations were insufficient to constitute an offense, that the alleged acts were not in interstate commerce and that the law applied only to misbranding in interstate commerce, and that, in any case, the applicable section, 301(k), is unconstitutional as being beyond the legislative power of Congress and an invasion of the police powers of the state.

In rendering his decision, Judge T. Hoyt Davis pointed out that "it is well settled that Congressional authority under the commerce clause includes the power to regulate intrastate activities which 'affect' interstate commerce or which are in the 'flow' of interstate commerce."

The Court emphasized that the House Committee report which accompanied the Food and Drug bill makes it clear that Congress intended to exercise this power in regard to misbranding of drugs. If 301(k) were not applicable, it was explained, misbranding provisions could be nullified by shipping properly labeled articles in interstate commerce and misbranding them after the transportation had ended.

"By the Federal Food, Drug and Cosmetic Act, Congress has sought to prevent the use of facilities of interstate commerce in conveying to and placing before consumers adulterated and misbranded articles," said Judge Davis. "That it may lawfully do this, the Court believes, is no longer open to question. Keeping within Constitutional limitation of authority Congress may determine for itself the means necessary to make its purpose effective. By section 301(k) Congress had exhibited the character of the means it deemed necessary to carry out its purpose, and the Court thinks it has kept within Constitutional bounds."

The Court held that it was not necessary to consider in this case whether or not the tablets involved were actually in interstate commerce at the time the misbranding occurred, but pointed out that this might be construed as misbranding in interstate commerce. The deciding point here was that the misbranding took place in a situation set forth in 301(k), namely, "while such article is held for sale after shipment in interstate commerce."

Interpreting this provision, the Court said: "In order to give effect to the purposes of the Act, the protection of the consumer, the prohibitions relating to the article must go along with it while it is being held for sale by anybody, whether the original interstate consignee, wholesaler, distributor, or retailer. The article in the hands of any dealer and until it reaches the ultimate consumer is being held for sale."

In deciding whether or not there had been an

actual misbranding, the Court concluded from an analysis of 301(k) and labeling regulations thereunder that there was "no room for doubt that the acts charged are within the meaning and purpose of the statute."

In general, the Food and Drug Administration now permits use of the prescription legend only on products for which adequate directions and warnings cannot be devised to make them both safe and efficacious when used by laymen. As a practical matter, the pharmacist therefore had no alternative but to use sulfathiazole tablets only for prescriptions.

Judge Davis took occasion to point out that the prescription-legend regulations "require the drug to be sold on a physician's prescription and to bear the directions for use specified in the prescription." He specifically held that "the 'prescription legend' is not a substitute for adequate directions for use."

This statement also has significance in regard to manufacturers' labels on over-the-counter products. It seems to preclude a possible legal loophole—sought by at least one manufacturer—on the assumption that the legend itself constitutes the required "adequate directions for use" on drugs that are not harmful when used by the layman. If this were permissible, the legend would again become meaningless, as it often was under the old regulations. FDA's position, under the October 1945 regulation, is that the legend must be reserved as a warning to pharmacists that a product is not safe or effective for self-medication.

PHARMACY'S ROLE IN POSTWAR ARMY

PLANS for more efficient and extensive use of pharmacists in the Army Medical Department have been submitted to the War Department General Staff by Maj. Gen. Norman T. Kirk, the Surgeon General. That the Army's postwar plan also calls for incorporating the Pharmacy Corps into a proposed Medical Service Corps is confirmed in the following statement released from the Office of the Surgeon General:

In Gen. Kirk's plan legislation will be sought to organize a Medical Service Corps which will place the Pharmacy, Sanitary and Medical Administrative Corps under one table of organization. Provisions are made for a pharmacist officer to serve in the Office of The Surgeon General. That officer will act as adviser to the Surgeon General on all pharmacy matters and will direct pharmaceutical activities of the Medical Department.

Utilizing pharmaceutical training and aptitudes to the utmost, pharmacist officers will be charged with the purchase, examination, shipment, storage and standardization of the drugs and medical supplies required by the Army. They will coordinate the preparation of supply tables and aid in preparation of standards of drugs and medical supplies.

In command functions they will be placed in charge of all types of medical supply depots as well as subordinate positions in the depot. And they will be named assistants to surgeons in battalions and regiments, as commanders of headquarters and battalion units, adjutants, medical and general supply officers and laboratory officers in medical and general laboratories.

No little part of their future duties will be instructing at training schools. Pharmacy officers will be especially sought in Regular Army commissioned ranks for duty in the postwar Army, which will require three officers of their capabilites for every thousand men. About 1500 will bring table of organizations up to strength in servicing the contemplated 500,000 peacetime Army strength. It is thought that additional duties given pharmacists will release other Medical Department officers from administrative duties.

Further, pharmacists will be qualified to serve in multitudinous hospital capacities as pharmacy officer, executive officer, adjutant, supply officer, mess officer, registrar, evacuation officer, hospital detachment commander and detachment of patients commander. They will compound and dispense medicines in units as large as General Hospitals and Hospital Centers.

In strictly combat organizations, the pharmacists will assume more authority than ever before. They will serve as medical and general supply officers to medical groups and battalions and command ambulance units.

In procurement jobs they will deal with contracts, purchase, inspection, shipment, storage, testing and standardization of medical equipment. Further, pharmacists are playing vital roles in administrative positions in the Office of The Surgeon General.

Gen. Kirk stated that pharmacy officers will receive the same pay, emoluments and retirement benefits as other officers of similar grade and length of service in the Regular Army. Promotions in field grade will be, as in the case of other branches, consistent with need.

FOOD AND DRUG CONTROL

40TH ANNIVERSARY OF LEGISLATION MARKS INCREASED SIGNIFICANCE TO PUBLIC HEALTH OF U. S. COMMUNITIES, WITH GOALS EXTENDED TO ACHIEVING EFFECTIVE WORLD COOPERATION IN POSTWAR HEALTH FIELD

by THOMAS PARRAN

SURGEON GENERAL, U. S. PUBLIC HEALTH SERVICE AND PRESIDENT, INTERNATIONAL HEALTH CONFERENCE

FORTY years ago when the Pure Food and Drug Bill was before the 59th Congress, many of the industries which some of you represent were opposed to the proposed legislation. In 1938, however, the same industries backed the greatly strengthened Federal laws governing the content, labeling and standardization of food, drugs and cosmetics. And finally, today, a professional association representing the same industries regulated by the Pure Food and Drug Law, celebrates the anniversary of that law.

We in the Public Health Service, like you of the food and drug industry, long have recognized the determining influence of Dr. Harvey Wiley in shaping the basic legislation. He consistently supported the principle that safeguarding the purity and strength of foods, drugs and biologics is a proper and important function of government on behalf of the people.

The record shows that the Marine Hospital Service, predecessor to the Public Health Service —and at that time the only Federal health agency —actively urged the enactment of the original food and drug law. In addition, the Public Health Service since 1902 has been directly responsible for the licensing of biologic products. In this work it has developed a relationship which, over a period of years, represents one of the outstanding examples of cooperation and mutual understanding between industry and government.

All of these mileposts in the legislative history of drugs and biologics control mark very real contributions to the public health. Through them untold sickness and death have been prevented that otherwise would have occurred. Our success to date has generated a public confidence that is as sobering as it is gratifying. You in industry and we in government are looked upon as guardians of the public health, and we have the joint responsibility for maintaining and strengthening the safeguards already established, and for developing new ones as needed.

The signs along our road point out quite clearly the value of industry-wide adoption of self-imposed standards in advance of restrictive legislation. They indicate also, as you can testify through your own industry balance sheets, that a philosophy of business practice based upon the welfare and protection of the consumer contains a major element of success.

The original Food and Drug Law was an important landmark in health legislation. The fortieth anniversary of the law comes at a time when we can count great gains along these lines. Today there are no less than 170 measures before the Congress concerned directly or indirectly with health.

They deal with medical care, mental health, medical research, dental research and service, a nation-wide network of hospitals and health centers, the training of health personnel, the prevention of stream pollution, and many other important problems. They are tangible evidence of the people's demand for public health and medical care programs strong enough to make greater inroads against sickness in our land, and make them more quickly than we have in the past.

We cannot afford to be complacent about our food and drug standards, nor in a larger sense, about our public health achievements as a whole. We are faced with the challenge of keeping pace with the swift moving frontiers of science and with the expanding social concepts of man's responsibility to promote the well being of his fellow man. New drugs and biologicals are constantly being developed whose manufacture and distribution may require additional safeguards. Penicillin and streptomycin are but two of the most recent examples.

In our efforts to protect the public in the manufacture and sale of food and drugs, we cannot help feeling a deep concern over some of the advertising techniques promoting the sale of products to the general population. In this field standards self-imposed by the industries are urgently needed. I am referring particularly to the widespread use of extravagant claims and

promises held out or implied in drug advertising on the radio.

At almost any hour of the day, listeners may hear announcements offering relief for a wide variety of human ills. In many of these cases no factual information is supplied to limit the hopes that may be aroused by the appeals. Although the physician is referred to at times in glowing terms, there is too seldom any reference to the importance of seeking competent medical diagnosis or treatment. An announcement which recommends that a certain product be taken every morning and night by everyone over 35, or states that 3 out of 4 persons suffer from vitamin deficiencies which are correctable by taking X brand of vitamins, obviously is not in accord with the therapeutic needs of the population. These are only samples of a trend that in my opinion is reaching disturbing proportions.

In the American pattern any product which is to be sold widely must be advertised. Radio is an important medium. Often, however, the enthusiasm of the sponsor gets out of bounds.

In setting improved standards for drug advertising, radio can look to an excellent example. Some years ago the newspaper industry took aggressive action in cleaning up drug advertising in their columns. A few representative and socially conscious newspapers of the country led the way and most of the others since have followed. Today many papers go so far as to conduct surveys to be sure that advertised products conform to established standards.

It is not too much to hope—even to expect—that the radio industry will do the same or even a better job once the need for such action has been made clear. Radio's contribution to public service has been notable. It has contributed to the advancement of health knowledge among the masses of our people.

The establishment of safeguards in drug advertising offers another opportunity for public service. You who are so keenly interested in both the welfare of the drug industry and the rights of the common man might appropriately work out this matter with the leaders of radio and advertising.

The upsurge of action to protect the individual's health and promote his welfare is moving not only toward higher national goals, but toward world-wide goals calling for international planning and action in the field of health. Even now, there is convened here in New York an assembly of historic significance in the annals of public health and in which you have a very large stake. I refer to the international health meeting.

SURGEON GENERAL THOMAS PARRAN

This is the first general conference called under the auspices of the United Nations. It is the largest international health conference ever held, and the most representative. Health is an appropriate subject for the first general conference, since if full cooperation among the nations is not forthcoming in this field there can be little hope for such cooperation in more controversial fields. Inevitably, there will be some differences, but I am confident they will be resolved. The leading public health experts of the world are gathered here, and these first few days have been marked by a scientific and professional atmosphere.

The speed with which this meeting has been called following the signing of the Charter of the United Nations in San Francisco a year ago, testifies to the thoroughness of preliminary foundations. It testifies also to the practical value of previous international experiences in health agreements, even as limited as they were.

In 1851 the French government called an international conference to discuss uniform quarantine codes. Soon after the turn of the century there came into existence the Office International

d'Hygiene Publique and the Pan American Sanitary Bureau, which at the outset were concerned primarily with administering treaties dealing with the exchange of epidemic intelligence and preventing, through quarantine, the spread of disease from one country to another.

Later these two organizations expanded their programs into other important fields. The League of Nations established a Health Organization which was highly successful. At one time or another, important studies were sponsored in malaria, nutrition, rural hygiene, syphilis and leprosy. International exchange of students and health experts was fostered. And, as you all know, significant progress was made in the standardization of drugs and biologicals. This is a sound heritage of experience upon which the new international health organization will draw. The tasks ahead are great, but their accomplishment will bring great rewards.

Our government last year expressed its willingness to join the other major powers in sponsoring an international health conference and offered to act as the host for it. However, since the United Nations was being shaped so rapidly, it was agreed that the conference might more appropriately be held under its aegis.

Preparatory to the New York meeting, there was convened in Paris in March of this year, a technical committee commissioned by the Economic and Social Council of the United Nations to draft a preliminary charter for the proposed world health organization. It is this document which the health conference at Hunter College is now discussing.

The committee of experts which met in Paris proposed an organization sufficiently flexible and with enough authority to deal comprehensively with all international health problems, both those of an emergency nature and those endemic problems which are always with us.

Health As a Fundamental Right

A basic concept of the proposed charter, or constitution, is that health is a state of physical fitness and of mental and social well being, not only the absence of infirmity and disease; that the right to health is one of the fundamental rights of every human being, without distinction of race, religion, political belief, economic or social condition. This philosophy meshes at many points with that of the United Nations, which is dedicated to improved standards of living for all peoples, to a fuller life, a richer life. The fundamental freedoms can be realized and maintained only when people are healthy, well nourished and protected against disease.

The interdependence of nations in the field of health is widely recognized. The realization that lines on maps do not prevent the spread of disease is underscored time and again. The experience of any nation in the promotion of better health is of value to all other nations and, conversely, substandard health services and failure to control epidemics in any nation constitute a common danger.

International Objectives

Specifically, if the substance of the preliminary charter is adopted, the world health organization would, among other things:

Assist governments in strengthening their national health services, including loan of technical experts when requested to do so.

Assist in the development of an informed public opinion among all peoples on matters of health.

Promote more effective methods for the prevention of disease, the improvement of health and the extension of longevity through more intensive scientific research on an international scale.

Foster professional education through improved standards of teaching and training in health, medical and related fields by means of fellowships, courses, study tours and exchanges of visits.

Evaluate medical care plans and services from the point of view of both medical and hospital practice.

Promote, with the cooperation of other specialized agencies, the improvement of nutrition, working conditions, housing, and related environmental factors affecting health.

Standardize diagnostic procedures as desirable, and develop, establish and promote international standards for pharmaceutical, biological and related products.

In short, what we expect from the world health organization when it comes into operation is a dynamic world health center. Here, the most up-to-date knowledge of the world would be assembled on every subject pertaining to health, medicine and the related sciences. Here the nations of the world would go for information and for help.

We have come a long way since the early days when international health action was limited to quarantine against cholera, plague and smallpox. We are now on the threshold of a health concept that is universal in scope of action as

FDA'S FORTIETH ANNIVERSARY

The month of June marked the fortieth anniversary of the original Federal Food and Drug Act. At a commemorative meeting called by the Section on Food, Drug and Cosmetic Law of the New York State Bar Association, pharmaceutical leaders heard a series of papers and tributes concerning the work of the Food and Drug Administration and efforts to provide public protection in this field.

Surgeon General Parran, one of the guest speakers, paid tribute in the accompanying paper to achievements of FDA and pharmacy during the four decades, called attention to the need for further polishing of at least one facet of the pharmaceutical industry, and revealed extended horizons of global scope for health activities.

well as in geography. You can readily see, therefore, that the health problems to be encountered—in fact those already being encountered—cut widely across the relations between nations.

Many other international agencies touch the field of health. For example, the Food and Agriculture Organization is concerned, on a world-wide basis, with nutrition; the International Labor Office with industrial hygiene and social insurance; the civil aviation agency with the spread of disease through rapid transport; the Trusteeship Council with the health of dependent peoples; the Narcotics Commission with habit-forming drugs. It is to be expected that the world health agency will work with these and other agencies in technical matters and join with them in reaching a common goal. It is contemplated, also, that the Economic and Social Council of the United Nations will act as the co-ordinator to prevent overlapping and gaps in those fields with which two or more specialized agencies are concerned.

In the same way as official agencies are being brought into the over-all plans, so it is expected that leaders like yourselves will be asked to give the benefit of your interest and wise counsel when plans of international action are being formulated. The pending proposal which would strengthen and expand international standards for pharmaceutical, biological and related products should be gratifying to you. As experts, you can provide guidance and support for a constructive world-wide program to raise and maintain standards for foods, drugs and medical devices.

In approaching this objective, we are of course fully aware of the splendid work that has been carried on in the development of drug standards by the various nations through voluntary and public agencies. Here in the United States the official compendia recognized under our laws are the work of experts chosen by the respective medical and pharmaceutical organizations. The standards for drugs and biological products in these compendia are of the highest order. It is but natural, therefore, for us to feel that these standards should apply to products supplied for export or import trade, as well as to interstate commerce. As you know, there are some countries which have no standards at all for the manufacture, distribution and sale of drugs.

As a further objective, I hope we can agree that products failing to meet standards of the nation in which they are produced should not be dumped into international commerce. Such a policy would not only protect the public's health but also would promote sound international commerce and friendship.

Based on this premise, it is obviously desirable that minimum international standards be devised for drugs and biological products in common use.

In the matter of foods, a similar task awaits the appropriate international bodies. The nutritional aspects of the program might well be a joint undertaking for the Food and Agriculture Organization, and the world health organization.

Drug Standards

It is clear, therefore, that there is a need for further international teamwork in respect to food and drugs. Although a beginning has been made on the establishment of international standards, the job yet to be done is one of magnitude. The value of uniformity in the various national pharmacopoeias has been recognized for many years. The necessity for the unification of standards for drugs in universal use and for uniformity in strengths and formulas of preparations of drugs has been well recognized but requires further implementation.

A uniform system of nomenclature is likewise a basic consideration. It is particularly important

that in all countries the same name shall designate a drug of the same standard of strength and composition. Furthermore, it is important that the labels of drugs set forth clearly the standard under which the drug is sold. Differences in national standards and nomenclature are a drawback to the spread of medical and pharmaceutical knowledge. They cause serious difficulty for physicians and constitute a possible danger to patients. Let me give you an example of what I mean. Sulfanilamide is known by that name only in the United States. This identical drug is sold under more than twenty names in another country.

Another pressing international need in the field of our common interest is to compile and publish the food and drug laws of the different countries. At the present time these laws are not available in a central place nor in a single language. If they were compiled and published, together with other basic health laws and administrative health patterns of the various countries, an invaluable reference source would be established. This type of clearing house is one important element in establishing international biological and pharmaceutical standards.

Compiling the food and drug laws of all nations, and establishing uniform drug standards are but two of the initial steps that might be taken in a comprehensive program for the international standardization of food and drugs. Such a program is, in turn, but a part of the larger world health movement.

In the historic effort upon which we are now embarked I ask your encouragement and your support. While my topic has been the contribution which our food and drug laws have made to the health of our people, I could not overlook this timely opportunity to pay deserved tribute to you who represent the industry. Neither could I resist asking that we turn to the living future where so much depends upon our actions now.

An international opportunity impends. It is an international obligation as well—an obligation which falls heavily upon each of you. We have as our goal in the world health organization the same sort of teamwork between governments and industries that we have developed so effectively. We who are helping lay the foundations of world health look for the same guidance and help from the drug industry on an international scale as in meeting national problems.

ADDRESSES WANTED

MAIL addressed to the following A. PH. A. members has been returned by the post office. If any of our readers know the present address of any of those listed below it will be greatly appreciated if they will furnish us with this information.

Arnove, Forrest S. (Pvt.)
Alcott, Floyd M.
Alexander, E. E. (Cpl.)
Bennet, Rutherford A.
Belz, Richard Emil (Lt., jg, USNR)
Bisland, Merle E. (Lt.)
Bock, William H. (Sgt.)
Brown, Richard B. (Sgt.)
Brown, M. Elizabeth
Chavez, Marco A. (Pvt.)
Clark, William Walker
Coats, Oliver G. (C.Ph.M.)
Cole, Osco N. (Captain)
Cook, Frederick M.
Craft, Francis Edward
Cohen, Harry James (Sgt.)
Daniel, Sam H. (Sgt.)
Davidson, M. D. (CM3c)
Deutzer, Harry J.
Douglass, Frances
Eckstrom, Calvin W. (Sgt.)
Ellis, Francis R.
Featherstone, Lauren R. (T/-Sgt.)
Fichera, Alfio F. (T/Sgt.)
Finkelstein, M.
Fouch, Franklin Wheeler (Pfc.)
Frad, Gloria Anne
Friedman, William M. (Ph.M. 1/c)
Fulton, John D. (S2/c)
Gamboa, Ignacio Castro
Goldstein, David
Greenblatt, Eugene (Sgt.)
Gruz, Nathan I. (Lt.)
Gude, J. A., Jr. (Pharmacist, USNR)
Hachtel, Viola
Harris, J. W. (Lt.)
Hastings, Sidney S.
Henkin, Bernard (Captain)
Hershberg, Sheldon M. (Sgt.)
Jacob, Karl
Katz, Malcolm (HA 1/c)
Killackey, Frank
Konwiser, A. Lincoln
Landon, Frederick W.
Lazarus, Leon J. (Lt., jg)
Leckband, Theodore A.
Lerner, George G. (T/Sgt.)
Lindsey, Hugh (C.Ph.M., USN)
Louie, William L. (T/5)
Masunaga, George (Pvt.)
Metzger, Elmer W.
Mathis, Laurie
McPherron, Cecil L.
Moore, Mrs. Evelyn R.
Moore, Jessie T.
Nash, F. R.
Patterson, Duane R. (C.Ph.M., USN)
Potthoff, Orlando P.
Rau, Charles F. (A.S.)
Reeves, William I. (Lt.)
Richards, J. T. (Lt. Col.)
Sams, Ethel Wagner
Scarbrough, Carroll (Lt., jg)
Snow, Carmel M.
Schechter, Seymour
Schweig, Israel (Pfc.)
Shiigi, Kenneth
Stein, David
Stewart, Ollie R. (Ens., USMS)
Sumner, Walter H.
Svedres, Edward V. (Lt., jg)
Thompson, Barnard
Thompson, Charles
Taurozzi, Ralph (T/s)
Titus, Frank D., Jr. (Lt., jg)
Tolles, King O.
Tusing, Thomas
Vetrano, Carmine V. (Sgt.)
Williams, T. D.
Witt, Ewald
Zimmermann, L. Freeda
Zuber, A. J.

PLANS COMPLETED FOR MEETING

PLANS for A. PH. A.'s first postwar meeting are now being completed. Leading off the convention week program at Pittsburgh's Hotel William Penn will be the American Association of Colleges of Pharmacy, with the first session scheduled for 2 p. m., Sunday, August 25. The following morning (Monday) will mark the opening meetings of the National Association of Boards of Pharmacy and the Conference of Pharmaceutical Association Secretaries.

Tuesday, August 27, the first sessions of the American Society of Hospital Pharmacists and of the American College of Apothecaries get under way at 9 a. m.

Meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION itself start Tuesday afternoon, August 27 and continue through Friday, August 30. Outstanding speakers at the various sessions will include President George A. Moulton; President-elect Earl R. Serles; Dr. Paul B. Dunbar, Commissioner of Food and Drugs; Dr. Austin Smith, secretary of the A. M. A.'s Council on Pharmacy and Chemistry; Dr. E. C. Elliott, director of the pharmaceutical survey being conducted by the American Council on Education; Comdr. W. Paul Briggs, director of pharmacy service for the Veterans Administration; Dr. E. Fullerton Cook, chairman of the U. S. P. Revision Committee; Dr. Justin L. Powers, chairman of the National Formulary Committee; and Surgeon General Norman T. Kirk, U. S. Army.

Immediately preceding convention week, August 22 through 24, the Plant Science Seminar will hold its twenty-third meeting. The Roosevelt Hotel, at 6th St. and Pennsylvania Ave., will be the headquarters for the Seminar. The opening session is scheduled for 10:30 a. m., Thursday, August 22, at the Hotel.

This will be followed by a three-day program of lectures and field trips designed for those with a special interest in botanicals and plant life. Most of Saturday will be devoted to a botanizing trip to Ohiopyle, Pa., with Dr. O. E. Jennings, acting director and curator of botany at the Carnegie Museum of Pittsburgh, serving as guide.

A. Ph. A. Convention Committee

Plans to welcome American pharmacists to Pittsburgh, August 25–30, have been made by the following members of the Local Committee for the A. PH. A. convention:

Executive Committee: Hugh C. Muldoon (General Chairman), dean of Duquesne University School of Pharmacy; George D. Beal, chairman of the A. PH. A. Council; Edward C. Reif, dean of the University of Pittsburgh School of Pharmacy; Stephen Wilson (Local Secretary), professor of pharmacy University of Pittsburgh.

Finance and Budget Committee: James C.

HUGH C. MULDOON
General Chairman

STEPHEN WILSON
Local Secretary

Sims (Chairman), vice-president and director of the Sun Drug Co.; George D. Beal, assistant director of the Mellon Institute for Industrial Research; Robert R. Gaw, president of the McKennan Drug Co.; Joseph H. Laufe, retail pharmacist of Greensburg, Pa.; George L. McMillin, retail pharmacist and chairman of the executive committee of the Pennsylvania Pharmaceutical Association; Fred Schiller, retail pharmacist; John R. Thompson, chairman of the Board, Pittsburgh College of Pharmacy, and vice-president of the George A. Kelly Co.; George O. Yohe, president of George O. Yohe, Inc.

Entertainment Committee: Edward C. Neid (Chairman).

Reception Committee: William H. Whitman (Chairman).

Publicity Committee: W. John Davis (Chairman).

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STATUS OF RUTIN REMAINS UNCERTAIN

A REPORT OF THE COUNCIL ON PHARMACY AND CHEMISTRY, AMERICAN MEDICAL ASSOCIATION

RECENT newspaper articles announcing rutin as a "cure" for high blood pressure, based on a release from the United States Department of Agriculture, have again demonstrated the inadvisability of premature publicity concerning new medical discoveries. As a result of these articles the office of the Council on Pharmacy and Chemistry has received numerous inquiries concerning the properties and availability of this new drug.

The only published report in a scientific periodical about the clinical use of rutin at the time this statement was prepared, is a brief note by Griffith, Couch and Lindauer (*Proc. Soc. Exper. Biol. & Med.*, 55:228 [March], 1944) describing preliminary observations on 14 patients with increased capillary fragility treated with rutin. The authors concluded that "in certain cases rutin appears to have the property of decreasing capillary fragility in subjects in whom this fragility is initially increased."

Rutin is a glucoside found in a number of plants, the principal sources being tobacco and buckwheat. Laboratory investigations have been conducted by J. F. Couch and his associates at the Eastern Regional Research Laboratory of the United States Department of Agriculture at Chestnut Hill, Pa. The clinical work on rutin has been done chiefly at the University of Pennsylvania under the direction of Dr. J. Q. Griffith Jr. Although several firms are interested, no commercial production of rutin has been made.

Although newspaper accounts state that rutin is a treatment for high blood pressure, the Agriculture Department release stated that, "according to clinical observations at the Medical School of the University of Pennsylvania, rutin is effective in the treatment of conditions arising from high blood pressure associated with increased capillary fragility."

This is obviously quite different from saying that rutin is a treatment or "cure" for high blood pressure. Furthermore, rutin has not been demonstrated to have any effect on the blood pressure of animals or man. Also so few data have been presented on variability of capillary fragility in untreated cases of hypertension that assessment of the effect of therapeutic agents is still hazardous.

Based on the meager amount of scientific evidence that has been available, it is unfortunate that the hopes of thousands of sufferers from hypertension have been raised by irresponsible and premature publicity. Increased capillary fragility is not a common complication of hypertension, and the vascular accidents which are frequently the serious sequelae to this disease may not be due to alterations in capillary resistance. Furthermore, the methods of measuring capillary resistance are crude, and workers in this field are not agreed on the reliability of any of the methods of measurement now employed.

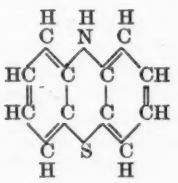
In considering the reports on rutin it is well to keep in mind the experience with "hesperidin," or "vitamin P," which was alleged several years ago to increase capillary resistance. Carefully controlled experimental and clinical studies on this substance failed to substantiate the claims advanced by the original proponents (Scarborough, Harold: *Lancet*, 2:610 [Sept. 10], 1938). It is to be hoped that history will not repeat itself in the case of rutin.

FIFTH SUPPLEMENT
to the
NATIONAL FORMULARY
SEVENTH EDITION

I. REVISION OF THE MONOGRAPH ON PHENOTHIAZINE, NATIONAL FORMULARY VII, PAGE 322

PHENOTHIAZINE
Phenothiazina

Phenothiaz. **Thiodiphenylamine**



$C_{12}H_9NS$ **Mol. wt. 199.26**

Description—Phenothiazine occurs as a pale greenish yellow to dark greenish gray powder, granules, or flakes. It is tasteless and has a slight characteristic odor. Phenothiazine is slowly oxidized when exposed to the air over a long period of time, the color becoming darkened.

Solubility—One Gm. of Phenothiazine dissolves in about 75 cc. of alcohol, in about 5 cc. of acetone, in about 20 cc. of chloroform, and in about 45 cc. of toluene at 25°. It is usually incompletely soluble in ether, and is insoluble in water.

Freezing point—The freezing point of Phenothiazine is not less than 179°, page 360.

Identification—

A: One drop of ferric chloride T.S. added to 10 cc. of an alcohol solution of Phenothiazine (1 in 2000) produces a green solution.

B: Add 1 cc. of hydrochloric acid to 100 cc. of water, heat to 80° and add 5 cc. of hydrogen peroxide T.S. Slowly add 20 cc. of an alcohol solution of Phenothiazine (1 in 100) to the well-stirred aqueous solution, maintaining the temperature at 80°: a deep red solution is produced, due to the oxidation of Phenothiazine.

Loss on drying—When dried over sulfuric acid for 3 hours, Phenothiazine loses not more than 1 per cent of its weight.

Residue on ignition—Phenothiazine yields not more than 0.2 per cent of residue on ignition.

Ether-insoluble substances—Completely extract an accurately weighed quantity of Phenothiazine in a Soxhlet extraction apparatus using absolute ether: the weight of the residue does not exceed 1.5 per cent.

AVERAGE DOSE (based on the weight of the animal)—

Horses and Mules, **30 to 50 Gm.** (approximately 8 to 13 drachms)
Cattle, **50 to 80 Gm.** (approximately 13 to 20 drachms)
Calves, **24 to 40 Gm.** (approximately 6 to 10 drachms)
Swine, **4 to 30 Gm.** (approximately 1 to 8 drachms)
Sheep and Goats, **25 Gm.** (approximately $6\frac{1}{4}$ drachms)
Lambs (up to 60 lbs.), **15 Gm.** (approximately 4 drachms)
Chickens, **0.5 Gm.** (approximately $7\frac{1}{2}$ grains)

Caution: Animals should be treated with Phenothiazine only upon the advice of a veterinarian.

Freezing Point of Phenothiazine

For the purpose of the National Formulary, the freezing point of a substance is defined as that temperature, approached by cooling a liquid, at which the solid phase is in equilibrium with the liquid phase. If supercooling does not take place, this is the lowest temperature remaining constant for a short period of time. In the presence of supercooling this point is the highest temperature remaining constant for a short period of time during the solidification of a substance from its molten state.

Apparatus Required—1. A pyrex test tube approximately 2.5 × 15 cm. to serve as a melting tube.

2. A larger pyrex test tube, 4 × 17 cm. to serve as an air jacket. The smaller tube is fitted through a cork stopper of such dimension that the tube may be inserted into the larger tube, telescope fashion.

3. Two 600-cc. beakers containing oil or other suitable bath fluid suitable for use at a temperature as high as 215°. The first bath is maintained at 210° ± 5°; the second at 175° ± 2°.

4. A ring stirrer made from a glass rod 3 mm. in diameter bent in such a manner that it fits into the smaller tube and permits free vertical motion around the thermometer.

5. A type II thermometer.

6. A watch or clock with a second hand.

Procedure—Fit the smaller test tube through the cork stopper and add about 5 Gm. of phenothiazine. Place in the bath at 210° and stir until the phenothiazine melts, then add successive 5-Gm. portions, melting each one with stirring before adding the next, until about 30 Gm. have been added or until the molten phenothiazine reaches the immersion mark on the thermometer. Place this tube inside the larger tube and immerse in the cooling bath at 175°. Insert the thermometer into the molten phenothiazine and stir continuously with the ring stirrer. After the sample has reached 185° remove the heat from the oil bath, or adjust in such a manner that the bath cools at the approximate rate of 1° per minute. While maintaining constant stirring of the sample, record its temperature every 30 seconds. If supercooling does not occur, the temperature will continue to fall until it reaches the freezing point when it becomes constant. After the temperature has reached the minimum, the recording of 5 consecutive readings establishes the end-point. In samples which exhibit supercooling, the end of supercooling will be indicated by a rise in temperature, and the highest reading obtained at the time of this rise is taken as the freezing point. Report as the freezing point the highest reading obtained after supercooling or the constant value obtained during the cooling period, estimated to the nearest 0.1°.

This Fifth Supplement to the National Formulary, Seventh Edition, is issued by action of the Committee on National Formulary, and with the approval of the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION. It is effective from June 15, 1946 until further notice.

JUSTIN L. POWERS, *Chairman*
Committee on National Formulary
American Pharmaceutical Association

Washington, D. C.
June 15, 1946

EDITOR'S NOTE: The Committee on National Formulary has authorized the revised monograph for phenothiazine given above since the assay and melting point specified in N. F. VII did not prove entirely satisfactory as official standards. The freezing-point determination authorized in the Supplement was found to be much more satisfactory as a method of controlling purity. Inaccuracies inherent in the colorimetric assay procedure did not permit differentiation between commercial "green" phenothiazine, N. F. and a more highly purified product. This and other considerations resulted in deletion of the assay from the revised monograph.

Reprints of the Fifth Supplement to the National Formulary may be obtained without charge by sending a self-addressed, stamped envelope to Justin L. Powers, Chairman; Committee on National Formulary, American Pharmaceutical Association, 2215 Constitution Ave., N. W., Washington 7, D. C.

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ELIXIR OF VITAMIN B COMPLEX

Can you find for me a formula for a syrup of the vitamin B complex suitable for administering to children?—A. C., Illinois

An elixir of vitamin B complex suitable for this purpose is prepared at the Charity Hospital pharmacy in New Orleans as follows:

ELIXIR OF B COMPLEX

[Makes 1000 fluid ounces (7 gallons, 6½ pints)]

Thiamin hydrochloride	2.000
Riboflavin	4.000
Vitamin B6 hydrochloride	.333
Calcium pantothenate	.362
Nicotinic acid	20.000
Alcohol	6 pints, 3 ozs.
Sugar	12 av. pounds
Butoben	94 gr.
Flavor	See below
Color	See below
Hydrochloric acid	See below
Water	6 gal., 1 pint

To 5 gallons 7 pints of water, add sufficient hydrochloric acid so that it will test *p*H 3.4. Dissolve the flavor in 5 pints of the alcohol and add it to the acidified water. Age for several days and filter with the aid of a small amount of talc. Dissolve the Butoben in 18 ounces of alcohol and add it slowly to the solution while rapidly stirring. Rinse the graduate with 1 ounce of alcohol and add it slowly while rapidly stirring. Add the nicotinic acid and the riboflavin and stir until dissolved. Dissolve the vitamin B6 hydrochloride in 10 ounces of acidified water. Dissolve the calcium pantothenate in 10 ounces of this liquid and add 155 mg. of tartaric acid. Dissolve the thiamin hydrochloride in 10 ounces of acidified water. Filter these solutions through three small filter papers. Drain. Wash each filter with 1 ounce of the acidified water. Add the three solutions to the above and mix thoroughly. Add the sugar and stir until dissolved. Add a sufficient amount of the color. Strain the preparation through damp canton flannel, smooth side down.

For color, we use a stock solution of 55 gr. Noka Brown (National) in 1 pint of distilled water. Only a few drops of this color per gallon of the preparation is required. For flavor, we use 1.5 ounces of a mixture consisting of 24 ounces oil of sweet orange, 2 ounces anethol, and 0.5 ounce of nutmeg.

PRESERVING EYE SOLUTIONS

Could you inform me of an effective means for the prevention of mold growth in stock solutions of $ZnSO_4$? These solutions are used in ophthalmic preparations.—A. S., New York

After investigating the preservative properties of several *p*-hydroxy benzoic acid esters, Arrigoni, Fischer and Tozer reported (*Arch. Ophth.* 26: 852–858, 1941) that a combination of the methyl and propyl esters is effective in low concentration. The combination finally selected was the

same as that used by Hasler (*Am. J. Ophth.*, 22: 423, 1930) and consisted of 65 parts of methyl-*p*-hydroxybenzoate and 35 parts of propyl-*p*-hydroxybenzoate. This mixture was used in 0.04% concentration.

Should you wish to obtain copies of the publications mentioned, the address of the *American Journal of Ophthalmology* is: Ophthalmic Publishing Company, 640 South Kingshighway, St. Louis, Missouri. *Archives of Ophthalmology* is published by the American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

STERILIZING INSTRUMENTS

A few physicians have asked me to compound for them a good, reasonable, sterilizing solution that is reliable and still will not rust their instruments. They are not interested in mercurial solutions. There is a newer type that interests me which I believe combines an alcohol radical with an ammonium salt. Could you furnish me with a formula so that I could make it in gallons?—D. H., California

The compounds to which you refer are no doubt the antiseptics of the quaternary ammonium type, represented by such commercial products as Ceepryn, Phemerol, Zephiran Chloride and Capacol. A paper on this class of antiseptics appeared in the August, 1945, issue of the *Scientific Edition* of THIS JOURNAL.

Chemical "sterilization" procedures, of course, have definite limitations no matter what disinfectant is used and cannot be relied upon as a safe technique. Steam heat under pressure (autoclave), or boiling water as a second choice, are preferred whenever heat would not affect the articles to be sterilized.

Gershenfeld points out in his book, *Bacteriology and Allied Subjects* (Mack Publishing Co., Easton, Pa., $6), that spores, especially if in a dry state, are not killed by chemical sterilization unless a prolonged exposure is used. In using the cold process, it is highly recommended that all articles first be mechanically cleaned to free them from blood and other organic matter or oil and grease.

In using the quaternary ammonium compounds it must be remembered that they lose their bactericidal activity in the presence of soap, protein and some of the newer detergents. Therefore, any traces of these substances must be washed from the instruments before immersion in the solution. When instruments are stored in solutions of quaternary ammonium compounds for long periods of time, Gershenfeld mentions that 0.5% of sodium nitrite is added to minimize corrosion.

Within the limitations mentioned, the quaternary ammonium compounds have been very favorably reported as cold disinfectants of medical and dental instruments.

A different type of disinfectant solution which is widely used is the Bard-Parker formaldehyde formula, compounded as follows:

Formaldehyde	3%
Alcohol	77%
Acetone	10%
Inert ingredients	10%

Tainter, *et al.*, have presented a paper on chemical sterilization of instruments in the *Journal of the American Dental Association* (31: 479, 1944) in which you may be interested. Copies of this journal may be secured from the American Dental Association, 222 East Superior Street, Chicago, Ill. They recommended the following as an acceptable formula, the ingredients being mixed in the order given:

Isopropyl alcohol	1000 cc.
Oil of rose geranium	2 cc.
Oil of cinnamon	4 cc.
Distilled water	780 cc.
Sodium nitrite	4 Gm.
Monoethanolamine	60 cc.
Solution of formaldehyde, U. S. P.	160 cc.

DELIQUESCENCE OF CALCIUM IODIDE

I would greatly appreciate it if you would assist me with the following problem in filling capsules consisting of:

Aminophyllin	*3 gr.*
Phenobarbital	*1/3 gr.*
Calcium iodide	*6 gr.*
Magnesium oxide (light)	*1 gr.*

Mix et make 30 capsules; D. T. D.

The contents of the capsule discolors and, because of the deliquescent nature of the calcium iodide, the capsules tend to stick together. —J. B., New York

Calcium iodide is, of course, very deliquescent and apt to change color rather promptly. Usually it is preferable to mix material of this nature with some magnesium carbonate which serves as an absorbent. We question this procedure in your prescription because of the possibility of

reaction with the calcium iodide. We would, therefore, suggest that the calcium iodide be placed in the smallest possible capsule and this inserted in a capsule of a larger size into which the additional ingredients could then be placed. The resulting capsule might be inconveniently large. It may be preferable to secure the prescriber's permission to divide the prescription, placing the calcium iodide in one capsule and the other ingredients in another, one of each to be taken at a time. The addition of a small amount of activated charcoal to the calcium iodide might give it sufficient color to mask any change in color which would develop later.

OINTMENT PRESERVATIVES

I mislaid the copy of the PRACTICAL PHARMACY EDITION *that contains the new hydrophilic ointment that will be made official. Could you please send me a copy of the article?*

Why did the formula contain two preservatives?—M. B., New York

We are asking Prof. Louis C. Zopf, who developed the hydrophilic ointment discussed in the December, 1945, issue, to send you a reprint.

As to the use of both methyl and propyl parahydroxybenzoate in this formula, each of these has a greater inhibiting action on certain microorganisms than the other. Therefore the use of two preservatives is more effective than either would be alone.

PROCAINE WITH PENICILLIN

Many physicians order procaine hydrochloride solution to be given with penicillin to make the administration less painful. The usual proportion ordered is 1 cc. of 0.5% procaine hydrochloride solution to one dose of penicillin. There has been a difference of opinion regarding the mixing of these two drugs. If the procaine hydrochloride solution is mixed in the vial with the penicillin solution and allowed to stand for several hours, does any notable change take place in either drug?—M. L., Missouri

Mixing procaine hydrochloride solution with penicillin to reduce pain apparently has been a fairly common practice. The difficulty seems to be, although you do not mention this, that a precipitate is thrown down upon standing.

We have been unable to learn what chemical reaction may occur, but apparently it involves impurities of penicillin rather than penicillin itself. Experiments have shown that the mixture of procaine hydrochloride solution with pure crystalline penicillin does not throw down the precipitate, and apparently no change occurs. When a mixture of commercial penicillin containing the precipitate was assayed, no loss of penicillin potency could be demonstrated. It is our understanding that, even though a precipitate may be present, such a mixture may be effectively and safely administered intramuscularly. Such a mixture of course must not be given intravenously, and the physician would want to take precautions in intramuscular administration that none of the mixture is injected into a vein.

If the mixture stands for some time before administration, there is also the possibility of hydrolysis of the procaine hydrochloride.

ATROPINE SUBSTITUTES

For some time I have been receiving inquiries from some of my physicians as to a formula which could be used to treat stomach disorders that are secondary to other nervous symptoms.

They have been impressed with preparations like Pavatrine with Phenobarbital and Trasentine with Phenobarbital, which have been presented to them as being of great advantage over atropine. However they are interested in a formula that they can write which will not have a trade name and which they can vary according to their needs.—A. N., New York

As your inquiry is primarily of a therapeutic nature, the following opinions have been secured from the office of the Council on Pharmacy and Chemistry of the American Medical Association:

Pavatrine and Trasentine are proprietary synthetic antispasmodics which are claimed to provide the desirable effects of atropine and papaverine without their undesirable side reactions. Neither of these proprietary products stands accepted by the Council on Pharmacy and Chemistry for inclusion in *New and Nonofficial Remedies*, and the firms which market them have not requested their consideration by the Council. At present the only Council-accepted atropine substitutes proposed for use in the alleviation of gastro-intestinal spasm are Novatropine (homatropine methyl bromide) and Syntropan (the phosphate of *dl* tropic acid ester of 3-diethylamino-2,2-dimethyl-1-propanol).

Based on the replies which we have received from three competent clinical investigators in the field of gastroenterology and pharmacology, to

whom your question was referred for comment, we present the following observations relating to the problem in which you are interested.

One consultant writes that the use of Pavatrine or Trasentine and phenobarbital combinations in the treatment of "stomach disorders that are secondary to other nervous symptoms" immediately raises the question of what is meant by "stomach disorders" and "nervous symptoms." The drugs used would of necessity vary with different types of stomach disorders. In many instances, correction of the "nervous symptoms" by means of a sedative such as phenobarbital alone would go a long way toward correction of the secondary "stomach disorders." As a matter of fact Pavatrine and Trasentine have little effect on the stomach and it is not improbable that the phenobarbital constituent accounts for much of the therapeutic value attributed to the combinations.

Another investigator expressed the following views:

"Another reason why many physicians give drugs like belladonna or atropine is that they hope to block the effects of stimuli coming down from the brain along the vagus nerves. After years of study in the laboratory of experimental physiology and after reading nearly everything on the subject in pharmacologic journals, I have very little faith in my ability with any drug to block these vagus or parasympathetic effects. I doubt if we could do it without at the same time drying up the mouth and seriously weakening accommodation in the eyes.

"My experience with the other drugs such as Trasentine and Pavatrine has not been anything to make me enthusiastic, and I have quit using them. If the combinations which you mention do any good, I think they help only because of the phenobarbital which quiets the person's excitable nerves.

"If I were to use a sedative and an antispasmodic, I would use the phenobarbital and let us say atropine separately, the better to judge of the effects which I got, if any."

From the foregoing information it would appear that the use of such combinations as Pavatrine with Phenobarbital and Trasentine with Phenobarbital for the treatment of so-called "stomach disorders that are secondary to other nervous symptoms" is of questionable therapeutic rationality inasmuch as certain disorders in this broad category often respond to phenobarbital alone. If variable combinations of atropine and the barbiturate do not satisfactorily fulfill the therapeutic needs referred to, the physician would seem to have only two other alternatives, namely, the employment of plain Pavatrine or Trasentine tablets with phenobarbital tablets separately or the substitution of one of the other synthetic atropine derivatives (Novatropine, Syntropan, etc.) for the Pavatrine or Trasentine constituent.

IRON-RUST STAIN REMOVER

What do you recommend to remove stains of iron rust?—J. C., Pennsylvania

The formula of a satisfactory stain remover of this type is given in *Pharmaceutical Recipe Book III:*

Cream of tartar	350 Gm.
Potassium binoxalate	350 Gm.
Oil of lemon	1 cc.

Mix the powders well and incorporate the oil of lemon.

Moisten the stained spot and rub with the powder.

DERMATITIS FROM PROCAINE

I seem to be allergic to Novocain. It causes a severe form of dermatitis and I have not yet found any coating to protect my skin. I wear gloves at the chair, but somehow the rash will begin at the glove top line and spread over the entire hand and wrist.—A. D., Alabama

Dermatitis due to procaine is not uncommon among dentists.

We understand that the use of rubber gloves solves the problem in most instances. It is unusual that the rash should spread over the entire hand despite this protective measure. An allergist in the U. S. Public Health Service, with whom we have discussed your query, suggests the possibility that you may also be allergic to the gloves. A dermatologist should be consulted for patch tests to determine just what the sensitizing agent or agents may be.

Experiments seem to indicate that sensitivity to procaine is highly specific in most individuals. Therefore some other local anesthetic of a similar type, such as tutocaine, might be used without difficulty. Even so, it should be kept in mind that sensitivity to these related compounds may also develop.

If you are not sensitive to rubber gloves and wish to continue to use procaine, it should be possible with some care to avoid contaminating the skin at the wrist with the solution. Sleeve guards that fit tightly over the glove at the wrist would provide additional protection. As supplied for use in industrial work, these are made of plastic fabric such as vinylite.

The Hospital Pharmacist

VALUE OF A WELL ORGANIZED FORMULARY*

by JAMES P. JONES

FORMERLY CHIEF PHARMACIST, UNIVERSITY OF CALIFORNIA HOSPITAL

A HOSPITAL formulary may be a most important adjunct to the efficient and economical operation of a hospital. This is often not appreciated until one considers what a formulary means to the doctor, nurse, pharmacist, patient and administrator.

The doctor is saved much time and many inconveniences by being able to refer to a pocket-sized formulary. The young internist especially finds the formulary a valuable guide of reliable information, while the visiting clinician refers to it often since it is a medium through which the various departments may indicate the professional services which are available.

This book should give information regarding X-ray examinations, drugs for diagnostic purposes, laboratory and clinical procedures and other helpful reference material as well as a therapeutic index with a list of reliable drugs and formulas. Such information will help give more patients attention and treatment with minimum delay.

To the nurse the formulary means a source of knowledge which will help orient her in the customs of the hospital. It is also a reliable reference in which she can check on new drug dosages and procedures.

The pharmacy probably will derive more benefit from the formulary than any other department of the hospital. This will be especially true if there are large clinics operated in conjunction with the hospital The pharmacy will not have to stock several items of the same pharmacological value, since the formulary usually suggests the use of drugs and preparations listed in the U. S. P., N. F. and N. N. R. or special formulas developed by the hospital staff.

With the necessity of having several brands or trade-marked preparations of the same drug eliminated, the pharmacist is able to purchase certain drugs in larger quantities at more favorable prices and there is an increased possibility of the pharmacy manufacturing a number of U. S. P., N. F. and special formulas at a considerable saving, often as much as 50 per cent or more. This is a very favorable factor tending to reduce the total pharmacy inventory and expense without sacrificing any of the professional service.

Another advantage is that the formulary will enable the pharmacist to anticipate the prescribing of certain preparations by the physicians. This gives the pharmacy a chance to have some preparations compounded and often packaged in convenient quantities for dispensing soon after the receipt of an order. Thus the pharmacist can render more and better service at less expense.

The patient is indirectly benefited by a hospital formulary through its effect on the efficiency, professional service and economy of the departments serving him. He should receive attention and treatment sooner than might otherwise be possible and he will also be able to have his prescriptions filled with reliable and fresh drugs, which can be compounded and dispensed with minimum delay and at the most favorable price. These factors, especially the professional service and the time and the expense involved, usually worry the patient and these are the factors which a hospital formulary may influence the most.

* One of a series, sponsored by the American Society of Hospital Pharmacists, currently appearing in the journal *Hospitals* to promote a better understanding of adequate pharmaceutical service among hospital administrators.

The value of the formulary to the administrator is its combined value to the above groups and this usually means a more efficient and economically operated hospital with the best professional service. The administrator or any one preparing a hospital formulary must be warned that there is a grave danger of just the opposite effect being obtained if caution is not observed in setting up a formulary and the policy regarding it. This danger comes from the very element of the formulary which may contribute most to an increase in efficiency and economy—the element of standardization.

A Pitfall

The danger is not from rational standardization but from too stringent a standardization of procedures and formulas and the degree of this standardization is dependent upon the institution and situation involved. Some institutions may inadvertently sacrifice professional service and efficiency for the sake of the greater economy which may be effected by a standardization in which the physician is restricted to an inadequate choice of drugs, formulas or procedures.

This may be exemplified by any situation in which the hospital staff is restricted to the use of only one member of each of the various classes of medication, such as one antiseptic, one general anesthetic or one local anesthetic. This is an extreme and absurd example, however, it serves to point out a situation which may prevail to a lesser degree if caution is not observed in setting up a hospital formulary. Too much emphasis cannot be placed on the fact that the hospital staff must have available any useful procedure, drug or formulas.

The task of compiling a formulary is usually the responsibility of the hospital pharmacy committee and any specialists who may be available. All sections of the formulary, however, should be reviewed by staff members interested in their contents and any comments or suggestions made by them must be given serious consideration. This will assure cooperation of the hospital staff in the ultimate use and establishment of the formulary in the hospital.

Generally, only U. S. P., N. F. and N. N. R. drugs or formulas should be admitted to the formulary, an exception being made in cases of drugs or preparations of outstanding value or those which have been found to be exceedingly useful in the institution compiling the formulary. Essentially, the formulary must be tailored to the hospital and the staff of doctors, nurses and pharmacists who are to use it in daily practice.

In compiling a formulary, the following topics may be considered and information given regarding them:

1. Prescription writing with a complete list of Latin abbreviations.
2. Size of prescriptions and orders which are most readily available.
3. Vehicles and colors.
4. Drugs subject to Federal and state regulations.
5. Buffered and isotonic solutions.
6. Table of *p*H indicators.
7. Tables of trade-marked preparations with their public names.
8. Antiseptics.
9. Drugs for diagnostic purposes.
10. Endocrine preparations.
11. The vitamins.
12. Available drug list.
13. Vaccines, serums and antitoxins.
14. Therapeutic index.
15. Hospital formulas.
16. Parenteral fluids with some of their uses.
17. Pediatric therapeutic index and procedures.
18. Well-baby clinic data.
19. Dental drug list.
20. Institution's dental drug formulas.
21. Charts indicating types of diets and their uses.
22. Average heights and weights.
23. Obstetrical data.
24. X-ray examination and consultations.
25. Laboratory and clinical procedures.
26. Common emergencies.
27. Treatment of burns.
28. Treatment of acute poisoning with a complete list of recognized antidotes.
29. Table of international atomic weights.
30. Sulfonamides and antibiotics.
31. Maximum safe doses of potent and dangerous drugs with emphasis on the irregularity of response and idiosyncrasy of the patient.
32. Sedatives and hypnotics.
33. Policy and purpose of the publication.
34. Index with adequate cross references.
35. A list of instruments and equipment with their location.

Frequent Revision Needed

Revisions of a formulary are very important and must be provided for as often as necessary. This should be at least as often as the revisions of the U. S. P. and N. F. If revisions are not made, the book soon loses its value and is worse than no formulary.

With the present rapid progress in medicine and pharmacy, it is advisable to revise a formulary as often as every two or three years. Even

with such short periods between revisions it is well to supplement the formulary with special bulletins which give complete information regarding new drugs, treatments or special procedures. This not only serves to keep the personnel well informed, but draws the attention of new staff members to the formulary and the services available in the hospital.

Those interested in further discussions and information regarding hospital formularies are referred to the report of the committee on pharmacy in the *Transactions of the American Hospital Association*, Vol. XXXIX—1937, and the papers on "The Formulary System" in the pharmacy section of the *Transactions*, Vol. XLII—1940.

Summary

The hospital formulary is discussed and its uses other than as a pharmaceutical guide pointed out. Various topics considered are:

1. Value of the formulary to the doctor, nurse, pharmacist, patient and administrator.
2. Standardization of drugs, formulas and procedures and the danger involved.
3. Possible contents of a formulary.
4. The necessity of frequent revisions of a formulary.

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ESTABLISH MINIMUM LIBRARY NEEDS FOR VA PHARMACIES

A minimum list of required books has been established for pharmacies in institutions of the Veterans Administration. The list coincides with the primary list for a basic library presented in the February, 1946, issue of THIS JOURNAL, except that the medical dictionary has been replaced by a compounding text from the supplemental list—either *Scoville's Art of Compounding* or Husa's *Pharmaceutical Dispensing*.

In addition, the Veterans Administration has advised pharmacists that the following journals are considered the minimum sources for current pharmaceutical data in their practice: JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION in both the *Practical Pharmacy Edition* and *Scientific Edition;* either *Drug Topics* or *American Druggist*, with price list; and the *American Professional Pharmacist*.

Establishment of minimum library requirements for pharmacies is the most recent step in the program of W. Paul Briggs, director of pharmacy service, to improve pharmaceutical facilities in the Veterans Administration.

COMMITTEES ON THERAPEUTIC AGENTS BEING SET UP IN VA

A committee on therapeutic agents is being established in each Veterans Administration hospital and home, W. Paul Briggs, director of pharmacy service, announces. A pharmacist will act as committee secretary, with the clinical director serving as chairman. In hospitals with consultant staffs, a member of the staff will be included on the committee. All new drugs of interest will be reviewed and recommended to the central office in Washington before they are stocked by an institution's pharmacy.

Under the plan, each drug approved by VA may be obtained directly from manufacturers by pharmacists, at the request of physicians. Manufacturers have been invited to keep pharmacists and physicians in VA hospitals informed concerning new drugs and preparations.

HOSPITAL PHARMACISTS ORGANIZE IN NEW JERSEY

New Jersey hospital pharmacists have organized a local unit of the American Society of Hospital Pharmacists. Miss Lena Cutler of Newark is largely responsible for bringing about the organization, which has been named the New Jersey Association of Hospital Pharmacists. Those interested in membership are invited to write to Miss Cutler at the Lutheran Hospital, Newark, N. J., for information.

Science News Capsules

"SHOOTING STARS" by the thousands will flash through the sky in the early morning hours of October 9, if expectations of astronomers are fulfilled. Although the magnitude of a meteoric shower is difficult to predict, the earth will on that date be plowing through debris from the Giacobini-Zinner comet, which will have passed by eight days earlier. The earth comes within only 135,000 miles of the comet's path.

USEFUL MAGNIFYING POWER of the electron microscope has been increased from 100,000 diameters to more than 200,000 diameters by an improved magnetic lens developed at the RCA laboratories. General use of such high resolving power must await solution of certain technical problems. Eventually it is expected that heretofore unseen structural details of larger molecules, viruses and living cells will be revealed to aid medical science.

A NEW DESK-SIZE ELECTRIC COMPUTER will cut tedious hours of mathematical work to minutes in physical and chemical research. It has a special facility for solving linear simultaneous algebraic equations, representatives of the Consolidated Engineering Corp. of Pasadena, Calif., reported to the American Institute of Physics.

THREE OUT OF FOUR BABIES born at the turn of the century could be expected to reach the age of 25, while today three-quarters of the newborn babies will reach the age of 57. Average expectation of life at birth today exceeds 65 years, almost 16 years greater than at the beginning of the century.

RAM JET, the "flying stovepipe," may propel high-speed aircraft of the future or power the weapons of another war at twice the speed of sound. With no moving parts and no precision machinery, ram jet is essentially a pipe with a small opening at the front and open at the rear. Air is scooped in and compressed by its own speed; fuel is injected and burned; the exhaust streams out the rear, providing a thrust like a rocket motor. The ram jet achieves speeds of 800 to 1500 miles per hour, but must be brought to high speed by "booster" devices before it can operate.

FIVE COLOSSAL STONE HEADS, one frowning and the others placidly viewing the world, have been brought to light in the jungles of southern Mexico. This archaeological find was discovered on the site of an Indian ceremonial center believed to have existed between 500 and 800 A.D. "Best group of monuments we have ever found," was the judgment of expedition leader Matthew W. Stirling of the Smithsonian Institution.

ALCOHOLICS may some day be able to use a treatment that will keep them from having "lost week ends." Dr. J. D. Reichard of the U. S. Public Health Service suggested to the American Psychiatric Association meeting that if a drug, such as amphetamine, can induce a change in mood and behavior in one type of mental patient, some other drug might be found to change the mood and behavior of the alcoholic. Search for this substance must be based, he said, on a better understanding of anatomy, chemistry, physics and physiology as they are related to human feelings and behavior.

SYNTHESIS OF CANE SUGAR for the first time has won the $5000 Sugar Research Foundation Prize for Drs. W. Z. Hassid, M. Doudoroff and H. A. Larker of the University of California.

ATOMIC POWER PLANTS could be ready to serve industry "within two years of the time the problem is seriously attacked," says Dr. Leonard I. Katzin, one of the scientists who helped develop the atomic bomb.

SUSCEPTIBILITY TO DENTAL CARIES seems to run in a family, very likely is inherited and may be sex-linked, Dr. Henry Klein of the U. S. Public Health Service decided from a study of 1150 families of Japanese ancestry at the Colorado River Relocation Center.

HAYFEVER probably can be best controlled by chemical treatment of the allergy-producing weeds rather than treatment of the patient. Weed killer 2,4-D sprayed over areas infested with ragweed—chief cause of hayfever—will kill the plants before they shed any pollen if applied at a very early stage of flower development.

HEXAETHYL TETRAPHOSPHATE is a new insecticide uncovered by U. S. scientific field teams in Germany. The chemical, now being produced by Monsanto, kills aphids and mites that can survive DDT. Apparently superior in some respects to nicotine sulfate commonly used against these insects, the new insecticide will be particularly welcome since nicotine sulfate has been in short supply.

NUTRIENT X, an unidentified food factor, appears to have the properties of a vitamin and apparently plays an important part in the "palatability" of foods. Work is going forward in the U. S. Department of Agriculture and other laboratories to isolate and identify the substance or substances that constitute factor X.

STERILITY in men may be cured in certain cases

by treatment with the vitamin B complex, Dr. Gerson R. Biskind of the University of California Medical School reported at the meeting of the American Society of Clinical Pathologists. When the body does not get enough of this vitamin, the liver is unable to destroy the female hormone although the male hormone is removed at the customary rate. This upsets the hormone balance normally present, with consequent symptoms including, in the male, some types of infertility.

VACCINE against Japanese B encephalitis will be supplied to U. S. troops serving in Japan. Production has been assigned to the Army Veterinary Laboratory because of its experience in making vaccine to protect humans against equine encephalitis.

DICOUMARIN may help patients with the incurable disease, multiple sclerosis, Dr. Tracy J. Putnam of New York and his associates reported at the recent meeting of the American Neurological Association. In a series of 26 patients, 23 were freed from new acute attacks while taking the drug, although symptoms already present were not changed.

ATOMIC RESEARCH BY-PRODUCTS have been successfully used to treat superficial skin cancers and warts, Dr. B. V. Low-Beer of the University of California Medical School reported to the American Radium Society. Using radioactive phosphorus, 98% effectiveness was achieved in 52 patients with basal cell carcinoma, and 100% effectiveness in 36 patients with hyperkeratosis. Although such treatment for these types of disease has not been claimed superior to X-rays, radium or surgery, it is much simpler to use.

PAIN OF ACUTE GLAUCOMA may be eased by injections of anesthetic to block the sensory nerves of the eye. Solutions of pilocarpine and physostigmine are used before and after the injection. Besides symptomatic relief, the treatment also puts the eye in excellent condition for surgery.

CANCER STUDIES have resulted in a "vaccine" made by linking equine albumin with coal-tar chemicals that apparently cause one type of cancer. When injected into rabbits, antibodies were produced against the coal-tar chemical injected and against chemicals of similar structure. Whether this means that the coal tar-albumin material will protect animals against cancer caused by coal-tar derivatives has not yet been determined.

SCRUB TYPHUS, one of the severest diseases encountered by the Army in the Pacific and Asia, can be successfully treated with para-aminobenzoic acid. Eighteen patients receiving PABA, and compared with 16 control cases, had fewer days of fever, less severe symptoms, fewer complications and shorter convalescence. The report has been issued by the War Department's U. S. A. Typhus Commission.

RADIOACTIVE ANTIMONY is being used to form antimony compounds for the study of this class of therapeutic agents at the National Institute of Health and the Carnegie Institution of Washington. Antimony and potassium tartrate was found to leave the blood stream rapidly and, in dogs, more than half of it is deposited in the liver, where it is broken down into an unidentified new compound. Therapeutic effectiveness may be due to the latter compound. The studies are revealing information of importance in treating filariasis and schistosomiasis, tropical diseases encountered by American troops in the Pacific theater.

NOTES FROM A. M. A. MEETING

GOITER due to overactivity of the thyroid gland can "very likely" be cured by a single oral dose of radioactive iodine instead of having the patient undergo a surgical operation, Dr. E. M. Chapman of Massachusetts General Hospital, Boston, reported at the San Francisco meeting of the American Medical Association. Of 46 patients treated, 35 responded to a single dose; two doses were necessary in three cases and three doses in five cases. Acute reactions to large doses resemble X-ray sickness.

A LIFE-SAVING OPERATION for children born with the aorta narrowed or completely closed was reported to the American Medical Association by Dr. R. E. Gross of the Children's Hospital, Boston. The narrowed portion of the big artery is removed and the cut ends sutured together.

ANIMAL ORGANS may be kept alive and functioning normally outside the body in a machine which was exhibited publicly for the first time by its inventor, Dr. J. A. Long of the University of California. The apparatus has a mechanical heart, lung and blood system. Simplicity, versatility and cheapness are advantages over previous methods of studying living organs outside the body and will enable individual scientists to use it.

DICOUMARIN, the anticoagulant, saved the lives of approximately 73 patients among 1686 undergoing surgical operations, Dr. E. V. Allen of the Mayo Clinic announced at the A. M. A. sessions. The 73 patients would ordinarily have been expected to die due to emboli.

PENICILLIN AEROSOL, administered as a spray, produces an excellent response in streptococcic and staphylococcic pneumonia, chronic bronchiectasis and acute sinusitis, Dr. M. S. Segal of Boston reported. In his experience it was not effective against colds and had limited value for chronic sinus disease and infective bronchial asthma.

STREPTOMYCIN has apparently cured two cases of tuberculosis of the bladder treated by Dr. F. H. Redewill of San Francisco, it was reported at the meeting. Use of the drug in sufficiently large doses and its use together with penicillin were suggested as methods of preventing development of streptomycin-resistant organisms.

NEW SULFONAMIDE PROMISING FOR INTESTINAL ANTISEPSIS

Clinical studies are now in progress which will confirm or deny evidence that 2-sulfanilamido-5-carboxythiazole may find a place among drugs used for intestinal antisepsis.

First synthesized about four years ago, this sulfonamide has been found to possess high antibacterial activity and is poorly absorbed from the gastrointestinal tract, thus resembling sulfaguanidine, succinylsulfathiazole and phthalylsulfathiazole. It occurs as white crystals, stable for at least two years in solid form. Since the sodium salts are highly soluble, effective concentrations in solution may be expected in the intestinal tract.

That there is little danger of crystals being deposited in the kidneys—a complication observed with some other sulfonamides—is suggested by the fact that any 2-sulfanilamide-5-carboxythiazole that is absorbed and possibly acetylated will be freely soluble in body fluids.

Reporting on pharmacologic and clinical experiments, Dr. Philip S. Winnek of the Pitman-Moore Co., Indianapolis, says that the compound showed appreciable activity *in vitro* against the colon-typhoid dysentery group of organisms, "being in general more active than sulfanilamide and sulfaguanidine, and in some instances equal to sulfapyridine, sulfathiazole, and sulfadiazine."

In vivo the effect on reducing the number of coli in the feces of dogs and man is called "very striking." The reduction of the number of coli appears to be more rapid and at a lower dose level than with succinylsulfathiazole or phthalylsulfathiazole, when compared with data in the literature.

Comparable results have been obtained by Harris and Finland, who found that in their hands 2-sulfanilamido-5-carboxythiazole was poorly absorbed, nontoxic, and effective against bacillary dysentery.

—*Science*, 103:720 (June 21), 1946

COUNTS 100 PILLS PER SECOND

An electronic device which counts and feeds tablets, pills or capsules to alternate packaging positions at rates up to 100 per second was demonstrated to pharmaceutical manufacturers at the 1946 Packaging Exposition by the Wilmotte Manufacturing Co. The device can be synchronized with automatic packaging equipment.

ADR

DENTAL REMEDIES RECENTLY ACCEPTED BY A. D. A. COUNCIL ON DENTAL THERAPEUTICS

DENTIFRICES†

Irrizol Tooth Paste: Composition: See Milk-I-Dent Dental Cream. Manufactured and distributed by Trade Laboratories, Inc., Newark, N. J.

† *Accepted Dental Remedies*, Ed. 11, p. 93.

Not Acceptable

PETER PAUL'S CHARCOAL GUM

In a report which may be consulted in full in the July 1 issue of the *Journal of the American Dental Association*, the Council on Dental Therapeutics announces that Peter Paul's Charcoal Gum is not acceptable as a dental remedy. According to advertisements of Peter Paul, Inc., the chewing gum contains activated charcoal, which is described "as one of the most amazing purifiers known to science... almost magical in the way it adsorbs impurities... and helps remove tobacco and other stains from the teeth."

Chemists of the Council point out that, while activated charcoal has many uses, "evidence to show that it is a useful or desirable ingredient of chewing gum is totally lacking." The Council also concludes that incorporation of charcoal of any variety has not been shown to add to any cleansing effects which the chewing gum may exert.

MOUTH WASHES

Routine use of plain water or isotonic solution of sodium chloride as preferred mouth washes is recommended by the Council on Dental Therapeutics in a report which appears in the July 1 issue of the *Journal of the American Dental Association*. It is suggested that dentists obtain "medicated mouth rinse mixtures from the pharmacist, using and prescribing such mixtures only when necessary..." The objective is to help "the patient realize that mouth washes marketed indiscriminately are not known to be useful or necessary in the maintenance of oral or general health.

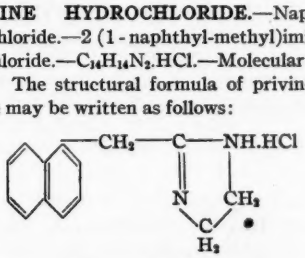
"The fact that many persons rely on medicated mouth washes when they should visit a dentist or a physician must result in numerous instances in serious delay in obtaining necessary treatment. For example, bad breath and sore throat are often symptoms of disease. The person who depends on mouth rinses to eliminate such symptoms or to prevent their development is fooling himself, perhaps to his own detriment."

NNR

PRODUCTS RECENTLY ACCEPTED BY THE A. M. A. COUNCIL ON PHARMACY AND CHEMISTRY

Council descriptions of drug products are published regularly in This Journal as they are accepted. Rules upon which the Council bases its action appeared in the July, 1946, issue (7:320, 1946) and may be secured in pamphlet form upon request to the Secretary, Council on Pharmacy and Chemistry, American Medical Association, 535 N. Dearborn St., Chicago.

PRIVINE HYDROCHLORIDE.—Naphazoline Hydrochloride.—2 (1 - naphthyl-methyl)imidazoline hydrochloride.—$C_{14}H_{14}N_2.HCl$.—Molecular weight 246.73. The structural formula of privine hydrochloride may be written as follows:



Actions and Uses.—Privine Hydrochloride is a vasoconstrictor, which, when applied to nasal mucous membranes, causes a prolonged reduction of the local swelling and congestion. It is of value in the symptomatic relief of disorders of the upper respiratory tract such as nasal congestion of allergic and inflammatory origin, acute and chronic rhinitis, vasomotor rhinitis and acute and chronic rhinosinusitis. Care should be exercised, however, when vasoconstrictors are used for prolonged medication; privine hydrochloride is no exception, although the rebound congestion of the mucosa which it may cause can be alleviated within a few days simply by discontinuing all nasal medication. Those who respond with rebound congestion may tolerate solutions weaker than the commonly used concentrations. The site of action is possibly the peripheral sympathetic nerve endings, a property assumed for epinephrine, although further work is needed to clarify this point. So far, there have been no reports proving that sufficient drug is absorbed following local application to increase the blood pressure, although this possibility should not be forgotten.

Dosage.—Adults may use several drops of the 0.1 per cent or 0.05 per cent solution, depending on the relief obtained and the sensitivity of the individual mucosa. Relief can be expected for several hours. Occasionally a smarting sensation and sneezing may develop.

For children, the 0.05 per cent solution is suggested.

Privine hydrochloride solution is buffered to a *p*H of 6.2–6.3. It is affected by aluminum and should not be used in atomizers made of this material. Otherwise the preparation can be employed by any of the conventional methods.

Tests and Standards.—

Privine hydrochloride occurs as a white, odorless, crystalline powder possessing a bitter taste. It is freely soluble in water and in alcohol, very slightly soluble in chloroform and practically insoluble in benzene and in ether.

Privine hydrochloride melts between 255 and 260° C. A 1 per cent solution of privine hydrochloride is clear and colorless; it has a *p*H of about 6.2 and responds to tests for chloride.

Place about 0.5 Gm. of privine hydrochloride in a separator, add 25 cc. of water saturated with sodium chloride and 5 cc. of 10 per cent sodium hydroxide solution. Extract the mixture with five 15-cc. portions of residue-free ether; wash the combined ether extracts with two 5-cc. portions of water; filter, and evaporate the ether solution to near dryness on a water bath. Remove the remainder of the ether in a stream of warm air and dry the residue at 70° C.; the melting point of a portion of the characteristic crystalline residue is between 117 and 120° C.

A 0.05 per cent solution of privine hydrochloride yields a white precipitate with phosphotungstic acid, a mauve crystalline precipitate melting at 158 to 160° C. with Reinecke's salt and a yellowish crystalline precipitate melting at 193 to 196° C. with picric acid.

Dry about 0.5 Gm. of privine hydrochloride, accurately weighed, for four hours at 70° C.: the loss in weight does not exceed 0.4 per cent. Incinerate about 0.5 Gm. of privine hydrochloride, accurately weighed: the residue is not more than 0.2 per cent.

Transfer about 0.2 Gm. of privine hydrochloride, accurately weighed, to a suitable Kjeldahl flask and determine the nitrogen content according to the method described in Methods of Analysis of the Association of Official Agricultural Chemists, fifth edition, page 26, art. 23: the amount of nitrogen is not less than 11.15 per cent nor more than 11.40 per cent when calculated to the dried substance.

Transfer about 0.2 Gm. of privine hydrochloride, accurately weighed, to a 400-cc. beaker and determine the chloride content according to the method as described in Methods of Analysis of the A. O. A. C., fifth edition, page 34, art. 49: the amount of chloride found corresponds to not less than 14.15 per cent nor more than 14.40 per cent when calculated to the dried substance.

Transfer about 0.2 Gm. of privine hydrochloride, accurately weighed, to a separator; add 5 cc. of water to dissolve the salt and then add 10 cc. of normal sodium hydroxide previously saturated with sodium chloride. Extract the mixture with six portions (25, 20, 15, 10, 10 and 10 cc.) of ether; wash the combined ether extracts with two 5-cc. portions of water; extract the water washings with two 10-cc. portions of ether and combine these extracts with the main ether extract. Evaporate the ether solution, contained in an Erlenmeyer flask, to near dryness on a water bath and complete the removal of ether in a stream of cool air; add 10 cc. of neutral alcohol to dissolve the residue, dilute to about 50 cc. with water and titrate with twentieth-normal hydrochloric acid, using methyl red as the indicator. Each cubic centimeter of twentieth-normal hydrochloric acid is equivalent to 0.01234 Gm. of privine hydrochloride: the privine hydrochloride content found is not less than 97.0 per cent.

CIBA PHARMACEUTICAL PRODUCTS, INC., SUMMIT, N. J.

Solution Privine Hydrochloride 0.1% (For Adults Only): 30-cc. and 480-cc. bottles. Each 100 cc. contains privine hydrochloride 100 mg., exsiccated sodium phosphate 258 mg., sodium chloride 324 mg., potassium chloride 223 mg. and potassium bisphosphate 742 mg., preserved with merthiolate 1:100,000.

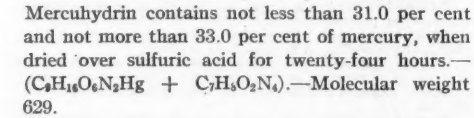
Solution Privine Hydrochloride 0.05% (For Children): 30 cc. and 480 cc. bottles. Each 100 cc. contains privine hydrochloride 50 mg., exsiccated sodium phosphate 258 mg., sodium chloride 331 mg., potassium chloride 223 mg. and potassium biphosphate 742 mg. preserved with merthiolate 1:100,000.

Privine Hydrochloride Nasal Jelly, 0.05%: 20-Gm. tubes. Each 1 Gm. contains naphazoline

hydrochloride 0.5 mg. in a buffered water soluble base containing glycerin, tragacanth and aromatics with merthiolate 0.01 mg. as a preservative.

MERCUHYDRIN.—Meralluride.—A mercurial compound derived from equimolecular quantities of mercurated allylsuccinylurea and theophylline.—Mercuhydrin contains not less than 31.0 per cent and not more than 33.0 per cent of mercury, when dried over sulfuric acid for twenty-four hours.—($C_9H_{16}O_6N_2Hg$ + $C_7H_8O_2N_4$).—Molecular weight 629.

The structural formula of the mercurated allylsuccinylurea, 1-(methoxy-oxymercuripropyl)-3-succinyl urea, may be written as follows:



Actions and Uses.—See Mercuhydrin Sodium Solution.

Dosage.—See Mercuhydrin Sodium Solution (THIS JOURNAL, 7:218, 1946).

Tests and Standards.—

Mercuhydrin occurs as an odorless white, crystalline powder, possessing a slightly bitter taste. It melts between 197 and 200° C. It is gradually decomposed by light, and is incompatible with hydrogen sulfide and fumes of strong acids. An aqueous suspension of mercuhydrin is acid to litmus.

Mercuhydrin is soluble in hot water but is practically insoluble in water, alcohol, chloroform and ether at 25° C.; it is soluble in glacial acetic acid, in aqueous ammonia solution and in sodium hydroxide solution. It is slowly soluble in sodium bicarbonate solution, with evolution of carbon dioxide.

Place about 0.5 Gm. of mercuhydrin in a small flask, add 5 cc. of water and 3 cc. of formic acid; boil the mixture under a reflux condenser for ten to fifteen minutes: a gray precipitate of metallic mercury is formed. Decant the hot solution through a small filter paper and allow the filtrate to cool (chill in ice water). Collect the crystals of allylsuccinylurea on a small filter paper, wash with two 5-cc. portions of ice water, allow to drain, and dry the crystals over sulfuric acid in a vacuum desiccator for twenty-four hours: the crystals melt between 145 and 148° C.

Heat the filtrate and washings obtained in the foregoing test to the boiling point and then pass hydrogen sulfide through the solution for ten minutes; filter, cool the filtrate; transfer to a small separator; add 10 Gm. of sodium acetate and extract with three successive 10-cc. portions of chloroform. Evaporate the combined chloroform extracts nearly to dryness on a water bath and complete the drying by means of a stream of warm air. Suspend the residue in 5 cc. of water, boil to dissolve the residue, filter while hot and cool the filtrate in a bath of ice water to allow crystallization. Filter, wash the crystals with water, allow to drain and dry in a desiccator over sulfuric acid for twenty-four hours: the crystals melt between 270 and 274° C. and respond to identification tests for theophylline.

Suspend about 0.5 Gm. of mercuhydrin in 5 cc. of sodium acetate solution and dissolve by the addition of just sufficient tenth-normal sodium hydroxide (about 8.5 cc.). Filter and divide the filtrate into two portions. To one portion add 0.2 cc. of sodium sulfide solution and compare with the other portion: only a very faint coloration of the test solution is noticeable immediately.

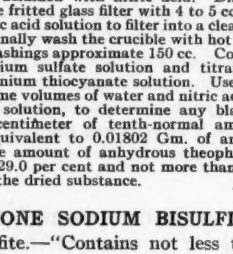
Dry about 1 Gm. of mercuhydrin, accurately weighed, over sulfuric acid in a vacuum desiccator for twenty-four hours: the loss in weight does not exceed 3.0 per cent.

Ignite about 1 Gm. of mercuhydrin, accurately weighed, in a porcelain crucible: the residue is not more than 0.1 per cent.

Transfer about 0.1 Gm. of mercuhydrin, accurately weighed, to a 50-cc. Erlenmeyer flask fitted with a ground joint, add 15 cc. of nitric acid and a few glass beads; connect the flask to a reflux condenser and heat to boiling for one and one-half hours. Cool; rinse the condenser tube with water, collecting the washings in the flask; transfer the contents of the flask quantitatively to a 400-cc. beaker and dilute to approximately 150 cc. with water. Add 5 cc. of nitric acid and titrate with fiftieth-normal ammonium thiocyanate, using 2 cc. of ferric ammonium sulfate solution as the indicator. Use a control solution containing 20 cc. of nitric acid and 2 cc. of the indicator solution in 150 cc. of water to which exactly 0.3 cc. of the fiftieth-normal ammonium thiocyanate has been added. Titrate the unknown solution to the same color intensity as the control and subtract 0.3 cc. from the volume noted in the titration. Each cubic centimeter of fiftieth-normal ammonium thiocyanate is equivalent to 0.002006 Gm. of mercury: the amount of mercury found is not less than 31.0 per cent and not more than 33.0 per cent, calculated to the dried substance.

Transfer about 0.7 Gm. of mercuhydrin, accurately weighed to a 250-cc. Erlenmeyer flask; add 125 cc. of water and 5 cc., of 10 per cent ammonia solution to dissolve the mercuhydrin. Add exactly 20 cc. of tenth-normal silver nitrate and warm on a steam bath until the white precipitate coagulates; cool to 30–40° C. and filter through a medium porosity fritted glass crucible, transferring the precipitate and washing with five 10-cc. portions of warm (40° C.) water until the wash water tests free of silver ion with sodium chloride solution acidified with nitric acid. Dissolve the precipitate on the fritted glass filter with 4 to 5 cc. of nitric acid; allow the nitric acid solution to filter into a clean flask without suction, and finally wash the crucible with hot water until the filtrate and washings approximate 150 cc. Cool; add 1 cc. of ferric ammonium sulfate solution and titrate with tenth-normal ammonium thiocyanate solution. Use a control containing the same volumes of water and nitric acid with 1 cc. of the indicator solution, to determine any blank correction. Each cubic centimeter of tenth-normal ammonium thiocyanate is equivalent to 0.01802 Gm. of anhydrous theophylline. The amount of anhydrous theophylline found is not less than 29.0 per cent and not more than 31.0 per cent, calculated to the dried substance.

MENADIONE SODIUM BISULFITE.—Menadione Bisulfite.—"Contains not less than 49 per cent of menadione ($C_{11}H_8O_2$)"—U. S. P.—Molecular weight, 330.29. Menadione Sodium Bisulfite has the following structural formula:



It may be prepared by the interaction of menadione and sodium bisulfite to form the addition product.

For description and standards see the U. S. Pharmacopoeia XII, First Bound Supplement, under Menadione Sodium Bisulfite and Menadione Sodium Bisulfite Injection.

Actions and Uses.—Menadione Bisulfite is used for essentially the same conditions as is menadione, which possesses the physiologic properties of vitamin K. Unlike menadione it is soluble in water, and stable aqueous solutions may be prepared.

Dosage.—It may be administered subcutaneously, intramuscularly or intravenously, the average daily dose being 0.5 to 2 mg. During administration of the drug the prothrombin level of the blood should be followed, especially when there appears to be need of an additional dose during a twenty-four hour period.

THE WM. S. MERRELL CO., CINCINNATI

Tablets Menadione Bisulfite: 3.84 mg.

Solution Menadione Bisulfite 3.84 mg. per cc.: 1-cc. ampuls. Each cubic centimeter contains the equivalent of 2 mg. of menadione, stabilized with 0.05 per cent sodium bisulfite.

U. S. Patent number 2,331,808.

CITRATED NORMAL HUMAN PLASMA (See New and Nonofficial Remedies, 1945, p. 535).

The following additional dosage form has been accepted:

SAMUEL DEUTSCH SERUM CENTER, MICHAEL REESE HOSPITAL, CHICAGO

Normal Human Plasma (Citrated): 60-cc. bottles. Phenyl mercuric borate 1;15,000 is used as a preservative; contains dextrose in final concentration of 5 per cent.

PROCAINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1945, p. 97).

The following dosage form has been accepted:

BARRY BIOLOGICAL LABORATORY, DIVISION OF BARRY ALLERGY LABORATORIES, INC., DETROIT

Solution Procaine Hydrochloride 2%: 30-cc. bottles. Each cubic centimeter contains procaine hydrochloride 20 mg., sodium chloride 4.4 mg., sodium bisulfite 1.0 mg. and 0.5 per cent chlorobutanol.

ESTROGENIC SUBSTANCES (See New and Nonofficial Remedies, 1945, p. 440).

The following additional dosage form has been accepted:

AYERST, MCKENNA & HARRISON, NEW YORK

Premarin (*Liquid*): 120-cc. bottles. Each 4 cc. contains 0.625 mg. of estrogenic substances (water-soluble) and 12.5 per cent alcohol.

PENICILLIN (See New and Nonofficial Remedies, 1945, p. 214).

The following additional dosage forms have been accepted:

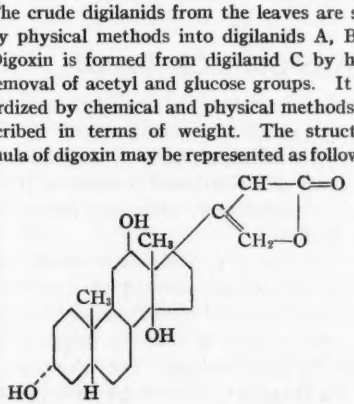
THE WM. S. MERRELL CO., CINCINNATI

Penicillin Sodium: 200,000 units.

E. R. SQUIBB & SONS, NEW YORK

Penicillin Sodium: 200,000 and 500,000 Oxford unit vials.

DIGOXIN.—$C_{41}H_{64}O_{14}$ (M. W. 780.92).—A crystalline glycoside which may be prepared from the leaves of Digitalis lanata or Digitalis orientalis. The crude digilanids from the leaves are separated by physical methods into digilanids A, B, and C. Digoxin is formed from digilanid C by hydrolytic removal of acetyl and glucose groups. It is standardized by chemical and physical methods and prescribed in terms of weight. The structural formula of digoxin may be represented as follows:



$(OHC.CH_2.CHOH.CHOH.CHOH.CH_3)_3—3H_2O$

Actions and Uses.—The actions and uses are closely similar to those of digitalis U. S. P. As a purified substance it is claimed to have particular usefulness when rapid digitalization is necessary, usually within a few hours when administered by mouth and within a few minutes when given intravenously.

Dosage.—Before administering the usual dose of digoxin, it must be ascertained that no drug of the digitalis group has been given within two weeks.

For rapid digitalization by the oral route, an initial dose of approximately 0.75 to 1.5 mg. may be administered, followed by doses of 0.25 to 0.75 mg. at six-hour intervals until the ventricular rate lies between 60 and 70, or the maximum therapeutic effect is obtained, or toxic symptoms appear. Patients who have received digitalis therapy during the preceding two weeks are given 1 mg. or less as an initial dose.

Very rapid digitalization may be accomplished with an intravenous injection of 0.75 to 1.0 mg. Ventricular slowing usually begins within a few minutes and is maximal in one to two hours. If complete digitalization is not obtained after six hours, additional doses of 0.25 to 0.5 mg. of digoxin may be given intravenously at six-hour intervals.

For maintenance 0.25 to 0.75 mg. may be given daily by mouth, or 0.25 to 0.5 mg. may be given intravenously.

Digoxin injection is a tissue irritant and the contents of the ampul should be diluted with 10 cc. of sterile isotonic solution. The product should be injected slowly (five to ten minutes) and care taken to avoid extravenous injection.

Tests and Standards.—

Digoxin occurs as a white, odorless crystalline powder, possessing a bitter taste (*care!*). When recrystallized from aqueous ethanol, it appears in the form of characteristic clusters of thin crystals. Digoxin is soluble in alcohol and pyridine but is practically insoluble in chloroform, ether and water. It melts with decomposition at from 255 to 265° C. when placed in a bath previously heated to 250° C.

Dissolve 1 mg. of digoxin in 2 cc. of glacial acetic acid containing 0.01 per cent of ferric chloride and add 1 cc. of sulfuric acid to form a subjacent layer: a pure brown ring, free from red color, is formed at the junction of the liquids. In a short time the acetic acid layer acquires an indigo-blue color (Keller-Kiliani test for presence of digitoxose).

Reflux 0.1 Gm. of dry digoxin with 10 cc. of alcohol, 10 cc. of water, 0.08 cc. of hydrochloric acid (specific gravity 1.16) for one-half hour. Neutralize the solution to litmus paper with 1 normal sodium hydroxide and evaporate to 2 cc., in vacuum; filter, dry the digoxigenin obtained at 80° C., and weigh (yield 45–46 per cent). When recrystallized from alcohol-water, the melting point of the product is 210–213° C. Dilute the filtrate from the hydrolysis to 25 cc., add 0.04 cc. of hydrochloric acid (specific gravity 1.16) and heat on a steam bath for twenty minutes. Neutralize the solution to litmus paper with sodium hydroxide solution and evaporate to a thick syrup in vacuum.

Dry the syrup in vacuum over sulfuric acid and extract the residue three times with anhydrous acetone. Evaporate the acetone and dry the residue in vacuum at 80° C. If crystals are not formed, allow the syrupy residue to stand in an ice chamber until crystals separate: the isolated crystals of digitoxose melt at 109–112° C.

Dry 0.1 Gm. of digoxin in vacuum over phosphorus pentoxide for four hours: the loss in weight is not more than 0.5 per cent.

The crystallographic and optical properties of digoxin may be summarized as follows: The crystals belong to the triclinic system; their crystalline habit is platy to tabular with rhombic outline, characteristically appearing with one acute angle or corner truncated. The crystals are biaxial, positive, with moderate optic angle. The refractive indexes are $\alpha = 1.522$, $\beta = 1.550$ and $\gamma = 1.610$. Birefringence is positive $(\gamma - \alpha) = 0.088$. Dispersion, $r > v$, weak.

BURROUGHS WELLCOME & CO., INC., NEW YORK

Tabloid Digoxin: 0.25 mg.

Solution of Digoxin, 0.05 per cent W/V: 30-cc. bottle. Each cubic centimeter contains 0.5 mg. of digoxin in 70 per cent alcohol solution.

Hypoloid Digoxin Injection, 0.05 per cent W/V: 1 cc. Contains 0.5 mg. of digoxin per cubic centimeter in 70 per cent alcohol solution.

THEOPHYLLINE ETHYLENEDIAMINE (See New and Nonofficial Remedies, 1945, p. 388).

The following dosage forms have been accepted:

BARRY BIOLOGICAL LABORATORY, DIVISION OF BARRY ALLERGY LABORATORIES, INC., DETROIT

Solution Aminophylline: 0.50 Gm. in 2-cc. and 20-cc. ampuls and 0.25 Gm. in 10-cc. ampuls.

G. D. SEARLE & COMPANY, CHICAGO

Aminophylline Supposicones: 0.50 Gm. Each suppository contains aminophylline, 0.50 Gm., incorporated into a suppository base consisting of a polyethyleneglycol of high molecular weight (Carbowax 4000 W) and propyleneglycol stearate (Emcol PS-50).

WYETH INCORPORATED, PHILADELPHIA

Suppositories Aminophylline: 0.5 Gm.

PENICILLIN (See New and Nonofficial Remedies, 1945, p. 214).

The following dosage forms have been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Penicillin Calcium: 100,000 and 200,000 Oxford unit vials.

BRISTOL LABORATORIES, INC., NEW YORK

Penicillin Calcium: 20-cc. vials. 100,000 and 200,000 Oxford units.

ASCORBIC ACID (See New and Nonofficial Remedies, 1945, p. 622).

The following dosage form has been accepted:

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Tablets Ascorbic Acid: 10 mg., 25 mg., 50 mg. and 100 mg.

PENICILLIN (See New and Nonofficial Remedies, 1945, p. 214).

The following dosage form has been accepted:

PREMO PHARMACEUTICAL LABORATORIES, INC., NEW YORK

Penicillin Sodium: Vials containing 100,000 Oxford units.

A REPORT OF THE COUNCIL

Potencies of Vitamin A Preparations.—From time to time the Council office has received inquiries from manufacturers as to the acceptability of vitamin A preparations in dosages of potency ranging from 50,000 units to 150,000 units or more. The Council has previously accepted no dosage of potency higher than 25,000 units. The Council believes that this policy should be continued. In reaching this conclusion, the Council is not concerned with toxic effects of vitamin A from the administration of capsules of higher potency. This view is based on the fact that to encourage the use of very large doses of vitamin A would not be in the interest of good medical practice. If those interested in doing investigational work desire to experiment with daily dosages of the order of 50,000 to 150,000 or more units they may use multiples of a 25,000-unit dosage. The Council finds no justification for routine administration of doses in excess of 25,000 units per day.

THERAPEUTIC TRIALS COMMITTEE

Completion of plans to facilitate clinical investigation of drug products through a Therapeutic Trials Committee has been announced by the Council on Pharmacy and Chemistry (*J. Am. Med. Assoc.*, 131:596, 1946). Full information on the purpose, organization and procedures of the Committee is available in reprint form on request to the Council secretary.

Sixteen leading medical scientists compose the group which will function as a standing committee of the Council on Pharmacy and Chemistry. It will provide a medium for bringing together drug manufacturers and competent independent investigators, help to coordinate clinical research and facilitate the exchange of advice among those working in the same field. Researchers are promised freedom of investigation and publication of their results, with certain provisos. Reaction to the plan has been favorable as a means for improving and speeding proper evaluation of the many new therapeutic agents now being developed.

AIR TRANSPORT FOR DRUGS

New speed in the delivery of drugs and medical supplies was presaged by inauguration of air freight service undertaken jointly by the Railway Express Agency and Northwest Airlines on June 1, with drug manufacturers promising extensive use of the facilities.

Another variation of postwar air transport for pharmaceuticals was demonstrated when a drug-laden "sky train" took off from Philadelphia and arrived in Puerto Rico in time for delivery to pharmacists the next morning. The "sky train" consisted of a Douglas C-47 towing a glider, both of which carried cargo.

Colleges

Dr. Ernest Little, recently retired dean of the **Rutgers University** College of Pharmacy, has been awarded the first Oscar Singer Memorial Medal by the New Jersey Pharmaceutical Association. The award is made for outstanding achievement in promoting the welfare of New Jersey pharmacy.

Dr. Charles F. Poe, professor of chemistry at the **University of Colorado,** has been named dean of the University's College of Pharmacy. During the war Dr. Poe served in the Quartermaster Corps, holding the rank of colonel. He has earned recognition in both Army and civilian life for his work in food and drug chemistry. Dr. Poe replaces former Dean Homer C. Washburn.

Dr. Arno Viehoever, former faculty member at the **Philadelphia College of Pharmacy and Science,** has been appointed technical consultant for the government to coordinate an investigation of the German pharmaceutical industry. He has also served with the Coordinator of Inter-American Affairs, Foreign Economic Administration and as technical adviser to the Siamese government.

Dr. Edward A. Brecht, Jr., member of the National Formulary Committee, has resigned his position at the University of North Carolina College of Pharmacy to join the faculty of the **University of California** College of Pharmacy.

Prof. Curt P. Wimmer, associated with the **Columbia University** College of Pharmacy for forty years, has been designated Professor Emeritus of Pharmacy.

Dr. C. Lee Huyck has been appointed professor of pharmacy to succeed Prof. Wimmer at the **Columbia University** College of Pharmacy. A. PH. A. member Huyck has held several teaching posts, served as research chemist with Wm. S. Merrell Co., and, more recently was senior pharmacist with the Winthrop Chemical Co.

Dr. Elbert Voss, formerly of the University of Wisconsin, has been appointed associate professor of pharmacology at the **University of Oklahoma** School of Pharmacy.

Mary Postizzi, recent graduate of the **University of Connecticut** College of Pharmacy and past-president of the A. PH. A. student branch there, has joined the faculty as assistant instructor in chemistry.

NEW BUILDING FOR TEMPLE PHARMACY SCHOOL

WORK has begun on remodeling the spacious building that will be the new home of the Temple University School of Pharmacy. Built within the last fifteen years in downtown Philadelphia, the structure was obtained recently from the Federal government. Dean H. Evert Kendig announces that the new facilities should be ready for the September, 1947, term, when an enrollment of 400 students will be accepted. Plans are also under way for a graduate school of pharmacy.

On the first floor there will be a reception room and lounge with a tile floor and decorative pool, administrative offices for Dean Kendig and his staff, pharmacy museum, large library and book bindery, and auditorium seating 800.

The building's 200,000 square feet of space will be shared with the School of Dentistry, which will principally occupy the second floor. The Pharmacy School will also be located near the Temple University Medical School and Hospital.

The third floor includes pharmacy lecture rooms, all equipped for audio-visual education. Here also will be seminar rooms, laboratories and auxiliary rooms for research projects.

There will also be laboratories on the fourth floor, together with additional classrooms and a pilot manufacturing laboratory. Facilities include a student cafeteria and faculty dining room.

A number of units have been set aside for the graduate school, and Dean Kendig points out that the spacious building will permit expansion as needed.

NEW TEMPLE PHARMACY-DENTAL BUILDING

A. Ph. A. Branches

LOCAL BRANCHES

MICHIGAN—Don E. Francke has been elected president of the Branch for the coming year. Other officers are Eston P. Stout, vice-president; R. W. Klein, treasurer; Bernard A. Bialk, secretary; Belle Moskowitz, assistant secretary; and Ernest R. Jones, chairman of the Program Committee.

NORTHERN CALIFORNIA—At a meeting held in conjunction with the convention of the California Pharmaceutical Association, Dr. Windsor Cooper Cutting of the Stanford Medical School spoke on "New Drug Therapy." Dr. D. Harold Copp, University of California Department of Physiology, spoke on "Medical Aspects of Nuclear Physics." Dr. George A. Moulton, president of the AMERICAN PHARMACEUTICAL ASSOCIATION attended the meeting and discussed activities of the ASSOCIATION.

At the May meeting of the Branch, L. W. Varblow of McKesson & Robbins spoke on "Pharmaceutical Manufacturing." He outlined the changes that have taken place in pharmaceutical manufacturing since 1850 and stressed the important part the Food and Drug laws have played in improving standards.

NORTHWESTERN OHIO—The second annual banquet of the Branch was held on May 22. Prof. John Schwarz of the Department of History at Bowling Green State University was the guest speaker. Eugene Imholt, Branch president reported on organizational activities of the past year.

BALTIMORE—Dr. Robert P. Fischelis, A. PH. A. secretary, spoke at a well-attended meeting held at the School of Pharmacy, University of Maryland, on June 13. The subject of his talk was "Pharmacy in the Affairs of the Nation." W. Arthur Purdum presided at the meeting.

STUDENT BRANCHES

ST. JOHN'S UNIVERSITY—Types and uses of atomizers and inhalant nebulizers were discussed by a representative of the DeVilbiss Co. at the May 20 meeting of the Student Branch.

Officers have been elected for the coming school year. Due to a tie for the presidency, it was decided that Edward Chudnofsky would head the Branch until his graduation in February, 1947, with Irving Katz, the other candidate, to serve as president for the remainder of the year. Milton Chaite is the new vice-president; Sister Rose Dominici, secretary; and Philip Grob, treasurer.

UNIVERSITY OF KANSAS—The newly organized Student Branch at the University of Kansas has held its first election of officers, naming Ralph L. Miller as president; C. Warren Plummer, vice-president; Patti Sue McClatchey, secretary; and Alvin M. Johnson, treasurer.

BUTLER UNIVERSITY—"Now for Tomorrow," a sound film in color, was presented by Owens-Illinois Glass Company at a recent meeting of the Student Branch.

SOUTHERN COLLEGE OF PHARMACY—New officers of the Student Branch are Bryant C. Brady, president; and June Snoddy, secretary.

MONTANA STATE UNIVERSITY—Thomas Hodsdon was recently elected president of the student branch. Marguerite Bean is the new vice-president; Ruth Peterson, secretary; and Dorothy Kirscher, treasurer.

ATTEND THE CONVENTION

FROM THE SECRETARY'S JUNE DIARY

—3rd—

TODAY came officers of the A. PH. A. Sections and of the Society of Hospital Pharmacists, College of Apothecaries and Institute of the History of Pharmacy to discuss coordination of the program for the week of August 25. Among those present were Hill, Selby, Wyss, Hazleton, Ray Kelley, Stoll and Stephen Wilson. Absence of the invited representatives of the Secretaries' Conference was noted with regret. Splendid progress was made in coordinating time schedules as well as subject matter and all cooperating beautifully.

At night to dinner with Pittsburgh Convention Secretary Stephen Wilson at the Willard reviewing details for the coming meetings which he and the local committee have well in hand.

—4th—

Today a meeting at A. PH. A. Headquarters of the Drug Trade Conference Committee on Uniform Laws with Schlotterer, Barta, Hammer, Frailey, Newcomb and Hayman all making splendid contributions to the objective, which is uniformity in all legislation affecting pharmacy. A fine group to preside over. Conclusions reached on barbiturate regulations, veterinary remedy acts and caustic poison acts. Dates set for further meetings to settle the more controversial questions dealing with pharmacy laws and sales limitations. After the meeting enjoyed showing Newcomb, who did so much to help raise funds for this building, the latest developments in its upkeep and use. Late at the office finishing important routine and then on the 8:30 p. m. train to Columbus, O.

—5th—

Arriving on time at Columbus and greeted by M. N. Ford at the Neil House where the Ohio State Pharmaceutical Association was in session and moving along on schedule. A conference with Fraiberg, Wyss, Matousek and other Cleveland Branch members discussing local branch problems and then to lunch at the Deshler with Fraiberg and Ford, returning in time to the convention hall for the half-hour talk on "The Pharmacist's Responsibility in the Distribution of Drugs." And there were many questions from the floor which indicated special interest in the prescription warnings.

Later a long talk with Dean Christensen on many matters dealing with the A. PH. A. convention. After viewing the well-arranged drug exhibit with Pharmacy Board Secretary Ford, rushed off to make the 5:30 p. m. train for Atlanta. Much credit to Vic Keys for a smooth-working and well-programmed convention which kept him and his members busy and well informed throughout.

—6th—

Reached Atlanta shortly after noon and met at the Biltmore Hotel by Charles Evans, Russell Rainey, Dean Wilson and by Harold Darnell of Indiana who was also a speaker on the program of the Association of Food and Drug Officials of the United States. Much conversation on the Veterans Administration contract for pharmaceutical service and found these men enthusiastic and eager to help in working out a satisfactory program.

At 2:00 p. m. addressed the Association of Food and Drug Officials of the United States on the barbiturate question, surprising some of them with the evidence of lack of uniformity in state regulations on the subject. Later a long conference on many topics of mutual interest with Commissioner Dunbar and State Cooperation Director Queen, and secured Dr. Dunbar's promise to appear at the House of Delegates' meeting in Pittsburgh to discuss the application of the Federal Food, Drug and Cosmetic Act to retail pharmacy. Sorry to have to leave the annual dinner of this association in time to board the 8:30 p. m. train for Washington.

—7th—

Directly from the train at 2:00 p. m. to the headquarters building and found the desk piled high as usual, but yielding to cooperative treatment by the staff even though it was the last working day of the week. Now looking forward to a good night's rest after three nights on the sleepers.

—8th—

This was no "Saturday off," for there was work to do on a Council Letter and other important documents. The telephone busy much of the afternoon conversing with Council Chairman Beal, Treasurer Schaefer, Finance Committee Chairman Swain and with Commander Briggs who is making good progress in obtaining a V. A. allowance to enable state associations to employ necessary clerical help for

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—9th—

Again breaking the Sabbath to be ready for the meeting of the legislative committee tomorrow, which will take definite action on the barbiturate problem. A quiet day at the office with much additional routine disposed of, and then to a fine home-cooked dinner with Captain and Mrs. Deibert at their home in the hills of Arlington.

—10th—

A good attendance of the Committee on Legislation including Martin Adamo, Swain, Kantner and Hugo Schaefer; joined by Dr. Austin Smith and J. W. Holloway of the A. M. A. Unfortunately Chairman Winne was unable to attend because his state convention was in session; so reported for him on the barbiturate survey and proposed provisions of a uniform state bill. As the sections of the bill were given consideration seriatim it became evident that American medicine and American pharmacy will have no difficulty in reaching agreement on what shall constitute a uniform state act. A day well spent in the interest of medicine, pharmacy and the public.

—11th—

All day catching up with the accumulated routine and answering questions on matters of policy for the staff. To dinner at the Statler with J. J. Clark discussing most recent developments in surplus drug selling. Then back to the office to finish some pending problems dealing with ASSOCIATION finances, in company with Paul Nowell.

—12th—

All day at the desk with many a telephone call and discussing the Secretaries' Conference program with Secretary Clara Miller by long distance telephone.

—13th—

Much routine disposed of and final check made of the work of the stone masons who have been busy around the building for many weeks. Also giving final approval to furnishings for the recreation room for our women staff members and hoping that the A. PH. A. Women's Auxiliary will like what we have done sufficiently to want to sponsor this activity.

A long session with the attorney who is drafting the Uniform State Barbiturate Bill now that the principles have been agreed upon. Via telephone comes a message giving advance notice that President Truman expects us to act as an adviser to the U. S. Delegation to the International Health Conference beginning June 19 in New York City.

At 5:00 p. m. on the train to Baltimore meeting Baltimore Branch officers Purdum, Balassone, Hager, Black, Du Mez, Kantner and other Baltimore pharmacists who had arranged a dinner prior to the meeting of the Branch, which we addressed on "Pharmacy in the Affairs of the Nation." A good attendance at the College of Pharmacy and met many old and new Baltimore friends who listened respectfully even though the night was hot and humid. Back to Washington by midnight.

—14th—

During the morning a private showing of the Owens-Illinois film "Now For Tomorrow," which did not appeal particularly to the staff whose eyes are on the development of pharmacy as a profession and not as a trade. Later joining a meeting of the steering committee of the Committee on Status of Pharmacists in Government Service with Einbeck, Du Mez and Frates in attendance. Lunching at the building and working late with Lawyer Williams on the draft of a barbiturate bill.

—15th—

All this Saturday morning at the office and then on the noon train to spend the week end at home.

—16th—

On the return trip to Washington found George Merck as a fellow passenger bound for important conferences in high places the following day. It is fortunate for the government that there are still some high-powered industrialists willing to give time to aid their government.

—17th—

An unusually busy day even for a Monday because office hours had to be cut short so we could leave with the U. S. Delegation to the International Health Conference. Much telephoning and conferring on last-minute details with the staff and a protracted conference with Guy Warfield on the A. PH. A. employees' retirement plan.

At 4:00 p. m. on the *Congressional* to New York, meeting and conferring enroute with the U. S. delegates and advisers to the International Health Conference; arriving in the early evening at Hotel Astor which will be U. S. delegation headquarters, although some distance from United Nations meeting facilities at Hunter College.

—18th—

All day in the preliminary sessions of the U. S. delegation reading and studying manuscripts, instructions and rules of procedure and obtaining a general orientation in preparation for the official opening of the conference tomorrow. Fortunate to spend the night at Red Bank which is only fifty miles from New York.

—19th—

An early morning meeting of the U. S. delegation for final instructions and discussion. At 3:30 p. m. to the official opening of the International Health Conference temporarily housed at the Henry Hudson Hotel because United Nations headquarters are completely taken up with the Atomic Bomb Commission, the Economic and Social Council and other activities lasting beyond anticipated expiration dates.

It was an impressive sight to find the delegates of 51 nations gathered in one small place eager to discuss their health problems, and representatives from 16 more on the way, having been held up by transportation difficulties. All speakers emphasized the great opportunity of this International Conference to not only accomplish its own purpose but to furnish the medium for better international understanding

on many related problems. At night to meet Council Chairman Beal at the Chemists' Club for a review of A. PH. A. activities and convention plans while Conn and Louis were "fighting" under the flood lights a few miles away.

—20th—

Further sessions of the International Health Conference and finding Surgeon-General Parran of U. S. P. H. S. easily the most popular and respected international figure at the Conference, which fact was reflected in his unanimous election as its president. Returned to Washington on the *Congressional* and spent the evening hours catching up.

—21st—

Late in the morning conferring with Watson Davis and Science Service staff member on the possibility of A. PH. A. cooperation in supplying pharmaceutical information to South American publications. Keen interest in current drug problems brings many a request for information from sources which completely ignored pharmacy in earlier days.

—22nd—

Much routine activity and, after luncheon with the staff at the favorite nearby Virginia Hot Shoppe, a long session with the attorney who is making good progress in drafting the uniform barbiturate act, spoiling a Saturday afternoon but glad to see this problem nearing solution.

—23rd—

After Sunday morning spent in the office, reached home in time for dinner and a restful evening on the banks of the Shrewsbury River.

—24th—

Early to the International Health Conference which continues in New York, finding the delegates eager to curb unnecessary conversation and get down to the real business. Slow progress because all speeches must be translated into English and French, which are the official languages. Marveling at the work of the translators and interpreters whose memories and linguistic facilities are equally good. At night to the Chemists' Club for dinner with Treasurer Schaefer, disposing of much A. PH. A. business.

—25th—

After a morning session with the U. S. Delegation and some committee work, attended the 40th Anniversary Celebration of the passage of the Federal Food and Drugs Act of 1906 at the New York State Bar Association building with Charles Wesley Dunn presiding. To luncheon at the Lotus Club with United Drug Co.'s Edward C. Merrill as genial host and Justin Powers, Caspari and Delehanty as fellow guests. Then back to the F. & D. meeting where Surgeon General Parran delivered one of the major speeches of the day. After dinner to the final session where Parran presided and good speakers held forth; but the attendance had dwindled as might be expected with three long sessions on the same subject.

—26th—

Most of the morning and afternoon at plenary sessions and committee meetings of the Inter-

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national Health Conference interspersed with a luncheon at the Bryant Hotel with Dr. Walter Clarke of the American Social Hygiene Association discussing future programs of the A. PH. A. - A. S. H. A. joint committee. Then on the late afternoon train to Atlantic City arriving in time to speak at the annual dinner of the New Jersey Pharmaceutical Association on "Pharmacy in the Affairs of the Nation." And the audience did not tire noticeably. Glad to renew old friendships with New Jersey colleagues and greeting many visitors and guests of the Association. A restful rolling-chair ride on the boardwalk and then to bed.

—27th—

After an early breakfast with N. J. P. A. Secretary John J. Debus caught the morning train for New York, arriving at U. S. Delegation Headquarters in time to catch up with committee affairs. Late in the afternoon to the Lombardy Hotel for a dinner meeting of the executive committee of the Board of Directors of the American Social Hygiene Association at which a long agenda was disposed of.

PHARMACIST HAS SILVER STAR FOR GALLANTRY IN ACTION

Pharmacist Gallio J. Marzano of Terminal Island, Calif., a member of A. PH. A., received the Silver Star for his "devotion to duty, courage and disregard for personal safety" in action with the 11th Armored Division near Lavassalle, Belgium. On one occasion Lt. Marzano, while serving as an assistant battalion surgeon, "moved under artillery fire to a tank that had been hit where he removed the dead and wounded and administered first aid," his citation states.

"On 1 January 1945, the battalion suffered numerous casualties in boggy terrain. Evacuation vehicles being unable to reach the wounded, Lieutenant Marzano organized available tanks under heavy artillery and small arms fire and moved the men to safety."

WARNING ISSUED ON CONTENT OF AEROSOL INSECTICIDES

Pharmacists should be certain to check the composition of aerosol insecticides before stocking them, in view of warnings issued by the U. S. Department of Agriculture. This type of insecticide has become popular with civilians, after having proved its worth in the Army's aerosol "bombs."

To date the Department's Bureau of Entomology and Plant Quarantine has approved no formula for use by the general public of an aerosol

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containing more than 3% DDT. Aerosols with a larger amount of DDT may be harmful to humans and not any more effective against the flying insects for which they are intended. Labels which indicate that the aerosol has been manufactured under a license issued by the Department assure a purchaser that the formula also has been approved by the Department.

After a great amount of experimentation to arrive at a proper and safe formula for the aerosols, entomologists found that the gas should contain pyrethrum for most effective use against insects. However, many brands offered now contain small amounts of DDT in addition to the pyrethrum.

Such aerosols, containing pyrethrum with small amounts of DDT, or containing pyrethrum alone, are nearly perfect for use in enclosed places as killers of mosquitoes, flies, and other flying insects. Aerosol insecticides were designed specifically for this type of use. While an aerosol will kill many crawling insects its use against them is wasteful and uneconomical. The Bureau suggests that other insecticides be used for the control of household insects such as cockroaches, ants, or bedbugs.

STREPTOMYCIN CAN INCREASE INFECTIVITY

DEATHS from infection in mice increase rather than decrease when streptomycin is given at certain dosage levels. This puzzling effect, which has important implications, has been reported by Dr. Henry Welch and co-workers at the Food and Drug Administration. There seemed to be "no adequate reason" why such an effect cannot also occur in man.

"If such is the case," Dr. Welch observed, "the problem of proper dosage with this antibiotic is magnified tremendously . . . . The deduction that improper dosage schedules in conditions for which this drug is now being used may lead to undesirable results is entirely logical."

It is likewise logical, the report emphasized, that by recognizing this peculiar phenomenon and adjusting treatment schedules accordingly clinical cures might be achieved in conditions which now appear resistant to streptomycin.

To date the drug has been used with success in the treatment of hemophilus influenzal meningitis, tularemia and Gram-negative urinary tract infections. In the treatment of other diseases, such as typhoid fever and undulant fever, results have been unexplainably erratic. Against these latter two diseases, streptomycin is effective *in vitro;* but when given to patients, some are cured while others do not respond even to relatively large doses. In some instances physicians can suggest no satisfactory explanation of the failure.

A possible answer is the finding of the Food and Drug Administration that under certain conditions streptomycin actually increases the infectivity of the organism against which the drug is used. This discovery came about through puzzling inconsistencies in results from laboratory tests on streptothricin, a drug closely related to streptomycin. Laboratory workers observed that relatively high concentrations of the drug did not interfere with the activity of *Staphylococcus aureus* as much as somewhat lower concentrations did. Substituting streptomycin for streptothricin, and using *E. typhosa* for the test, they obtained essentially the same results.

To check this disquieting information further, Dr. Welch and his associates turned to experiments on mice. The mice were infected with typhoid, then given streptomycin by injection.

Starting with a low dose it was found that, up to a certain point, stepwise increases in the dose actually cause comparable increases in the number of mice that succumb to the infection. Within this particular dosage range the fatality rate for mice is higher than when none of the drug is administered. As the size of dose is further increased, the number of fatalities then begins to drop. When the dose is sufficiently high streptomycin protects the mice against typhoid infection and no deaths occur.

The dosage range that embraces both the disease-stimulating and the therapeutically effective concentrations was found to lie within relatively narrow limits. Moreover, the concentrations of the drug produced in the blood are the ones usually found in the blood of man at some time during treatment with streptomycin.

Experimental data indicate that repeated tests, employing more than 2000 mice, always gave similar results.

Although Dr. Welch suggests several possibilities as to why streptomycin, at certain dosage levels, increased rather than decreased the fatality rate in mice, the facts now available do not permit a definite explanation.

Preliminary studies indicate that a similar phenomenon may be demonstrated with penicillin, although at a different dosage level.

Collaborating with Dr. Welch in the investigations are Drs. C. W. Price and W. A. Randall.

SUGGESTS FORMULATION FOR TREATING DIARRHEA

Because of the Narcotic Bureau's appeal for conservation of narcotics, Pharmacist Ralph W. Englehardt of the Rochester State Hospital has devised the following formula to replace the favorite combination of paregoric and milk of bismuth for cases of diarrhea:

Pectin	8
Glycerin	10
Syrup	40
Benzoic acid	1
Water, hot	100
Amyl acetate	0.3
Alcohol	3
Amaranth solution	0.67
Magma bentonite, *q. s. ad*	1000

Rub the pectin with the glycerin, add the syrup, then incorporate quickly, with vigorous stirring, the benzoic acid which has been dissolved in the hot water. To this add the amyl acetate dissolved in the alcohol, then add the amaranth, and finally the bentonite. The product may be homogenized, although this is not necessary.

As used in the Rochester State Hospital, 1 or 2 ounces is given orally after each bowel movement. Each ounce contains bentonite 1.25 Gm., and pectin 0.24 Gm.

U. S. P. TRUSTEES MEET IN NEW HEADQUARTERS

Plans looking to publication of U. S. P. XIII before the end of the year, and the charting of a comprehensive program upon which to base admissions for the following revision, U. S. P. XIV, were among the subjects discussed at the recent meeting of the U. S. P. Board of Trustees. This was the first meeting to be held at the new U. S. P. headquarters, 4738 Kingsessing Ave., Philadelphia.

Robert L. Swain of New York and Adley B. Nichols of Philadelphia were re-elected by the Board as chairman and secretary, respectively, for the coming year.

Consideration was given to having U. S. P. XIII translated into Spanish. A number of Spanish-speaking nations now recognize the Spanish edition as their official Pharmacopœia, and others are considering similar adoption.

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Bactra-Tycin Ointment is effective in treating abrasions, infected wounds, impetigo, folliculitis and infected dermatitis.

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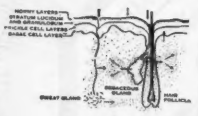

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